Southern Medical Journal

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SEPTEMBER 1959

VOLUME 52 NUMBER 9

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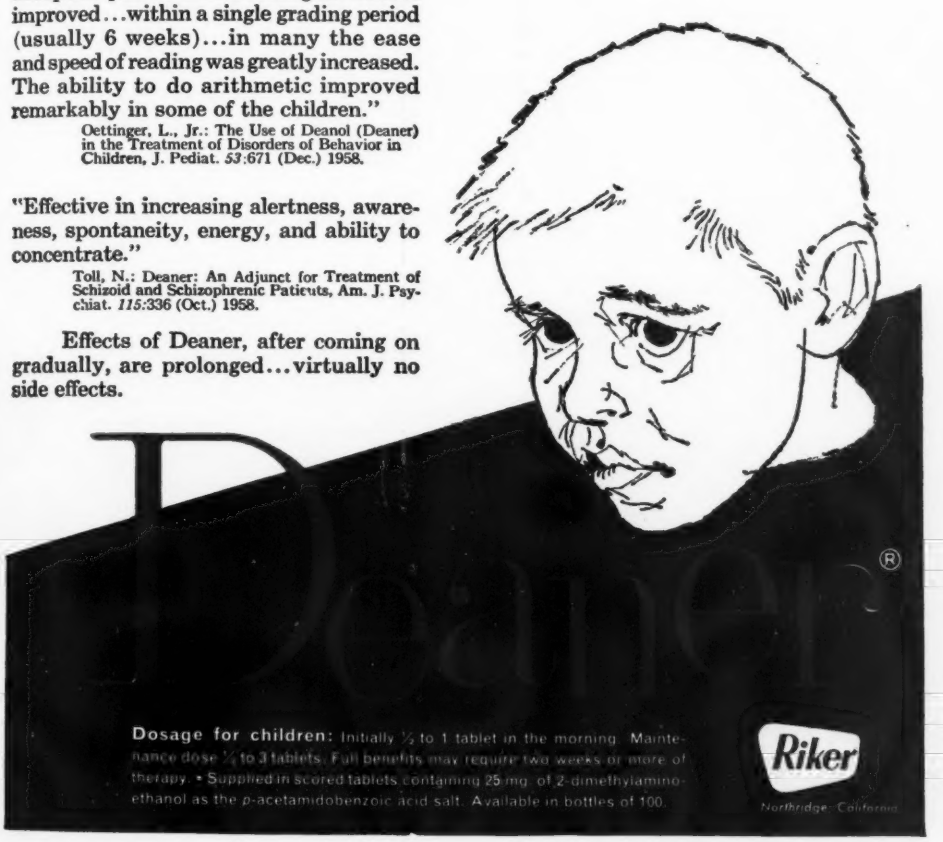

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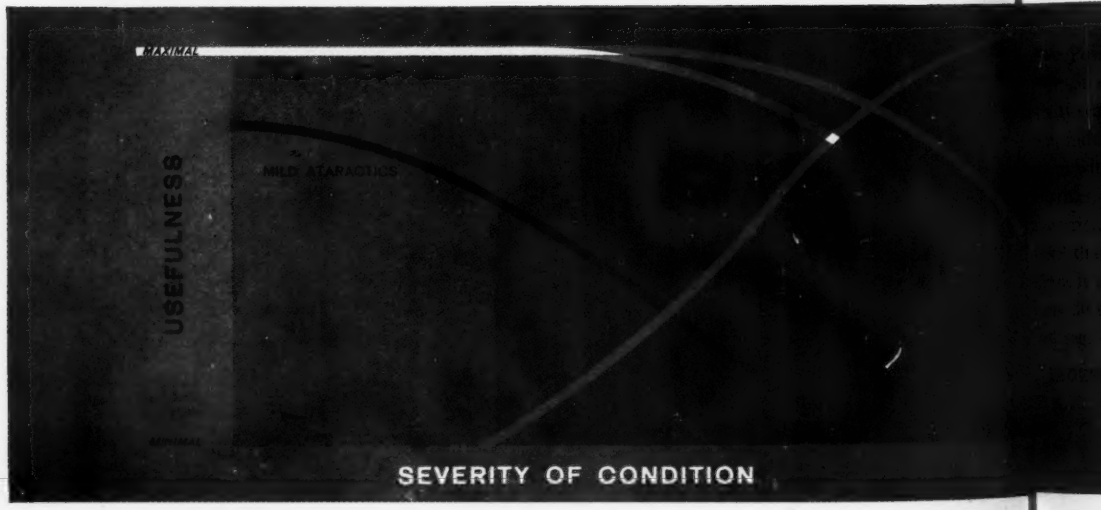

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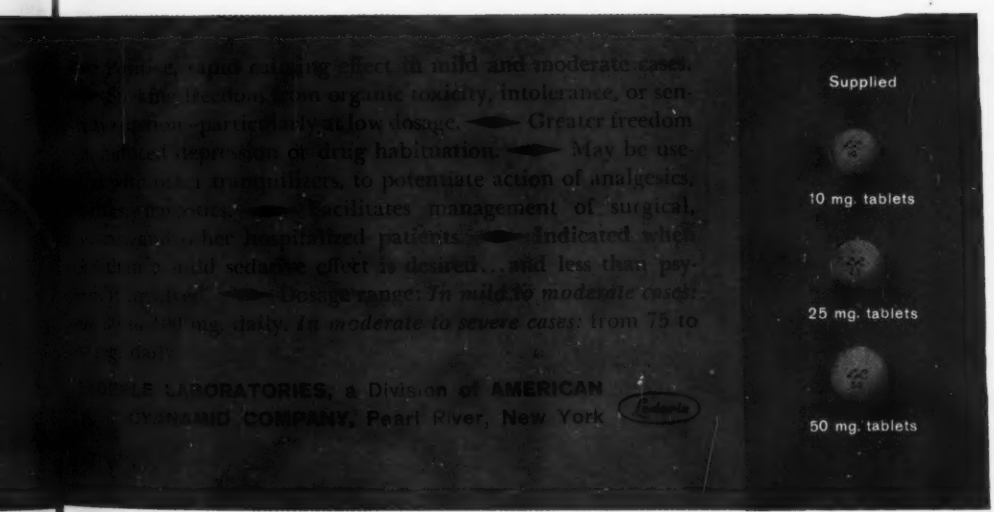

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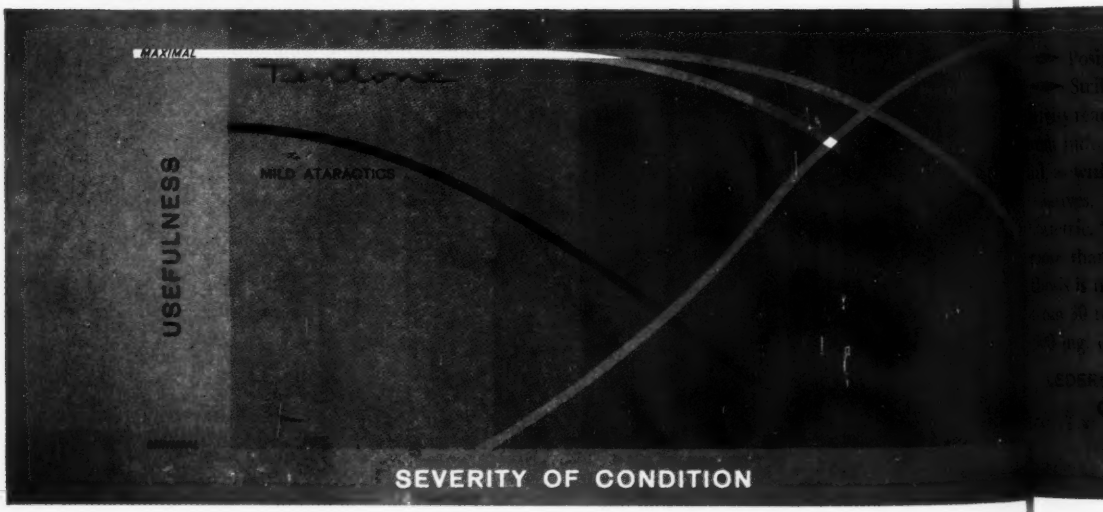

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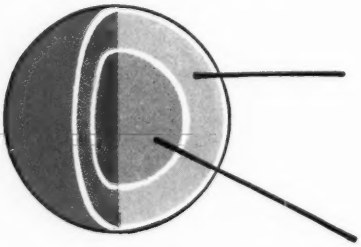

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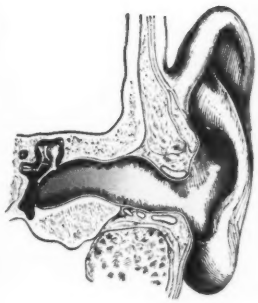

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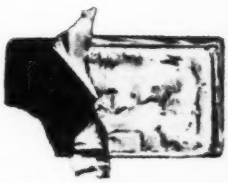

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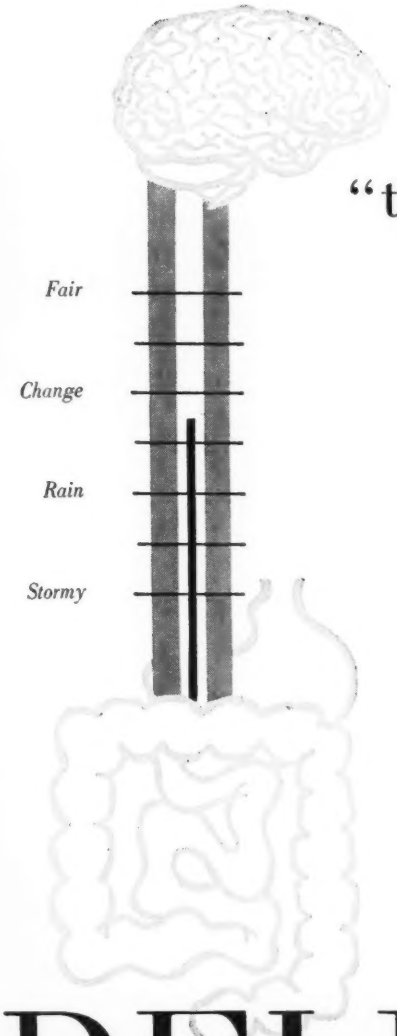

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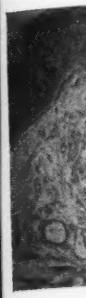

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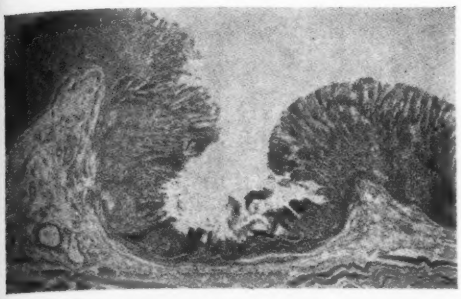
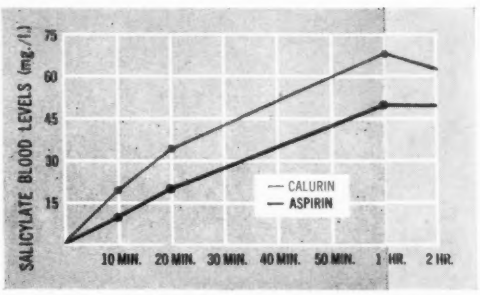


Particle-induced ulceration — section through lesion found in gastrectomy specimen. An aspirin particle was found firmly imbedded in this undermined erosion. Such lesions may be associated with the relative insolubility of aspirin, which remains in particulate form after dispersion in gastric contents.



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4. Flavored: can be chewed or dissolved in the mouth without water if desired — an advantage for patients requiring aspirin administration during the night and for pediatric patients.

Dosage: Each tablet of Calurin is equivalent to 300 mg. (5 gr.) of acetylsalicylic acid. For relief of pain and fever in adult patients, the usual dose of Calurin is 1 to 3 tablets every 4 hours, as needed; in arthritic states, 2 or 3 tablets 3 or 4 times daily; in rheumatic fever, 3 to 5 tablets 4 or 5 times daily. For children over 6 years, the usual dose is 1 tablet every 4 hours; for children 3 to 6 years, ½ tablet every 4 hours, as required. Not recommended for children under 3.

REFERENCES: 1. Waterson, A. P.: Aspirin and gastric haemorrhage, Brit. M. J. **2**:1531, 1955. 2. Douthwaite, A. H., and Lintott, G. A. M.: Gastroscopic observation of the effect of aspirin and certain other substances on the stomach, Lancet **2**:1222, 1938. 3. Editorial Comments: The effect of acetylsalicylic acid (aspirin) on the gastric mucosa, Canad. M. A. J. **80**:47, 1959. 4. Muir, A., and Cossar, I. A.: Aspirin and ulcer, Brit. M. J. **2**:7, 1955. 5. Muir, A., and Cossar, I. A.: Aspirin and gastric haemorrhage, Lancet 1:539, 1959. 6. Schneider, E. M.: Aspirin as a gastric irritant, Gastroenterology **33**:616, 1957. 7. Bayles, T. B., and Tenckhoff, H.: Salicylate therapy in rheumatic diseases, Scientific Exhibit, Ann. Mtg. A. M. A., San Francisco, Calif., June, 1958. 8. Batterman, R. C.: Comparison of buffered and unbuffered acetylsalicylic acid, New Eng. J. M. **258**:213, 1958. 9. Cronk, G. A.: Laboratory and clinical studies with buffered and nonbuffered acetylsalicylic acid, New Eng. J. M. **258**:219, 1958. 10. Editorial: Aspirin plain and buffered, Brit. M. J. 1:349, 1959. 11. Smith, P. K.: Plasma concentration of salicylate after the administration of acetylsalicylic acid or calcium acetylsalicylate to human subjects, Report submitted to Smith-Dorsey from Dept. of Pharmacology, Geo. Washington Univ. School of Medicine, Washington, D. C., Sept. 5, 1958.

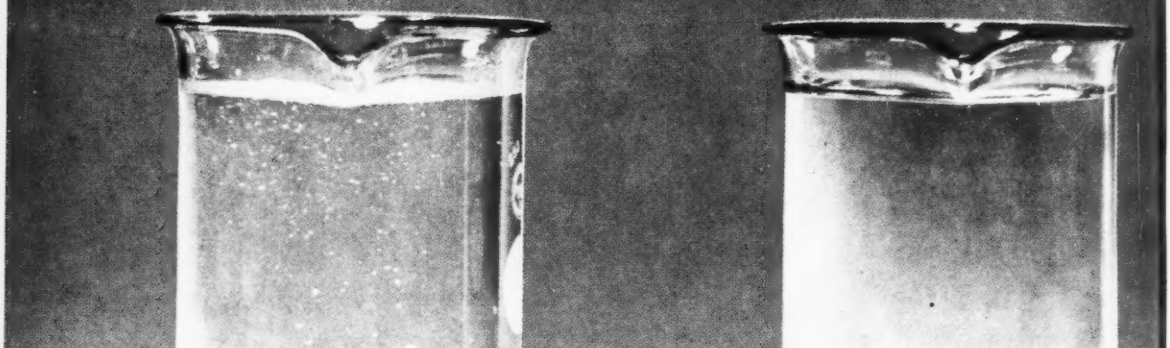
*TRADEMARK

SMITH-DORSEY • a division of The Wander Company • Lincoln, Nebraska

avoid the risk of insoluble, irritating aspirin particles

Chief among the drawbacks to aspirin usage is gastric intolerance. This ranges from mild upset and "heartburn" to severe hemorrhagic gastritis.[1-10] Studies performed in conjunction with gastrectomy[4,5] and gastroscopy[2] have shown insoluble aspirin particles firmly adherent to the gastric mucosa and imbedded between rugae. Reactions varying from mild hyperemia to erosive gastritis have been reported to occur in the areas immediately surrounding these adherent particles.[2,4,5] This is reported to be particularly true in patients with peptic ulcer.[4]

CALURIN is the freely soluble, stable calcium aspirin complex. Its high solubility forestalls gastric irritation or damage



Regular aspirin crystals 24 hours after being mixed into water.

Calurin crystals in solution one minute after being mixed into water.

STAE

Particle-i
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Dosage:
mg. (5 g
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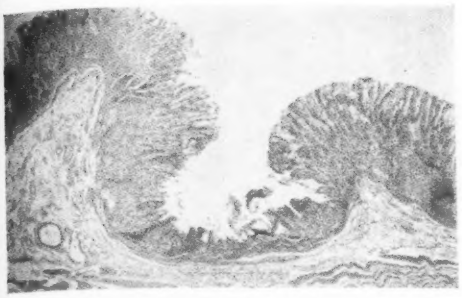
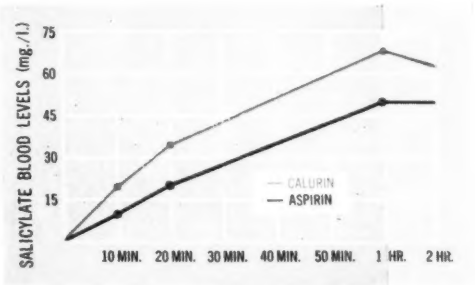
CALURIN*

STABLE SOLUBLE CALCIUM-ACETYLSALICYLATE-CARBAMIDE



Particle-induced ulceration — section through lesion found in gastrectomy specimen. An aspirin particle was found firmly imbedded in this undermined erosion. Such lesions may be associated with the relative insolubility of aspirin, which remains in particulate form after dispersion in gastric contents.



Calurin, being freely soluble, is promptly available for absorption into the systemic circulation. Salicylate blood levels in 12 subjects receiving both Calurin and plain aspirin were found to rise more than twice as high within ten minutes following Calurin. Also, these levels persisted higher for at least two hours.[11]

CALURIN is the aspirin of choice, especially when high-dosage, long-term therapy is indicated:

1. High solubility forestalls gastric irritation or damage. This advantage is of special importance in arthritis and other conditions requiring high-dosage, long-term therapy.
2. Produces high salicylate blood levels rapidly for prompt analgesic, anti-pyretic, anti-arthritic effect.
3. Sodium-free — for safer long-term therapy.
4. Flavored: can be chewed or dissolved in the mouth without water if desired — an advantage for patients requiring aspirin administration during the night and for pediatric patients.

Dosage: Each tablet of Calurin is equivalent to 300 mg. (5 gr.) of acetylsalicylic acid. For relief of pain and fever in adult patients, the usual dose of Calurin is 1 to 3 tablets every 4 hours, as needed; in arthritic states, 2 or 3 tablets 3 or 4 times daily; in rheumatic fever, 3 to 5 tablets 4 or 5 times daily. For children over 6 years, the usual dose is 1 tablet every 4 hours; for children 3 to 6 years, ½ tablet every 4 hours, as required. Not recommended for children under 3.

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*TRADEMARK

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Novahistine works better than antihistamines alone

Stuffy, runny noses...swollen, weepy eyes are more effectively relieved with Novahistine. The distinctly additive action of the vasoconstrictor and antihistamine combined in Novahistine relieves allergic symptoms more effectively than either drug alone.

one dose of 2 tablets for day-long or night-long relief. Each long-acting tablet contains Phenylephrine HCl 20 mg. and Chlorprophenpyridamine maleate 4 mg. Bottles of 50 and 250 green, film-coated tablets.

PITMAN-MOORE COMPANY Division of Allied Laboratories, Inc., Indianapolis 6, Indiana

Novahistine LP* LONG-ACTING

*Trademark

Thank You . . . . .

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For your continuing loyal support and confidence. It has done much to accelerate our phenomenal growth and strength in a surging southland, a tower of medical professions.

You've helped us . . . . .

- Grow into national prominence in the short span of three years.
- Expand from one . . . then two . . . now three . . . spacious buildings for manufacturing pharmaceutical products under the most exacting conditions . . . . 30,200 square feet in all.
- Erect our newest laboratory for development and control of all products fully manufactured by Carrtone.
- Staff our organization with skilled minds of highly proficient, technically trained personnel from some of the best universities.

A tip of our hat to you for all your contributions!

It will be our pleasure to welcome you when you visit our most modern laboratories.

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AN AMES CLINIQUICK® CLINICAL BRIEFS FOR MODERN PRACTICE

why is obesity a predisposing factor in diabetes?

In many people a high carbohydrate and low protein diet not only causes the obesity but also strains the carbohydrate-handling capacity. It is the long weight-gaining period that sets the stage for diabetes.

Source: Strang, J. M.: Am. J. M. Sc. *236*:405 (Oct.) 1958.

reliable results test after test...day after day

COLOR-CALIBRATED CLINITEST® BRAND Reagent Tablets

the *standardized* urine-sugar test for reliable quantitative estimations

standardized { *readings* / *"plus" system* / *sensitivity*

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COMPANY, INC
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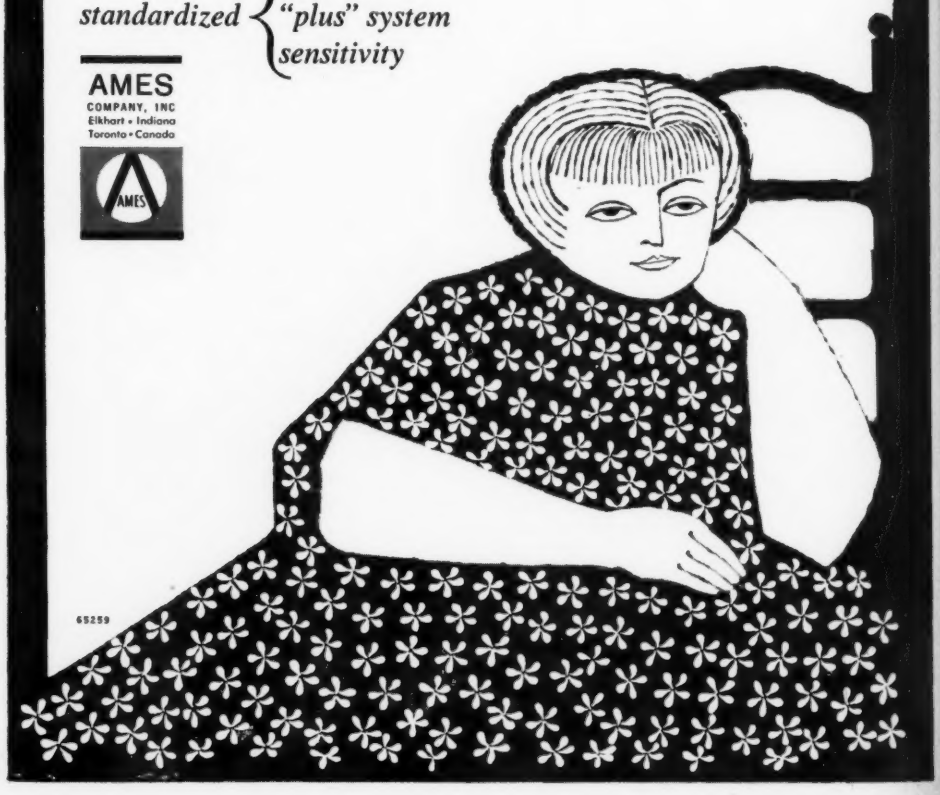


65259

THE **BUFFERED**
ACID VAGINAL DOUCHE
BUFFERED
TO **MAINTAIN**
AN ACID pH*

Mildly astringent soothing inflamed tissue

Low surface tension effectively penetrating vaginal folds

"Cleans" refreshing odor assuring patient acceptance

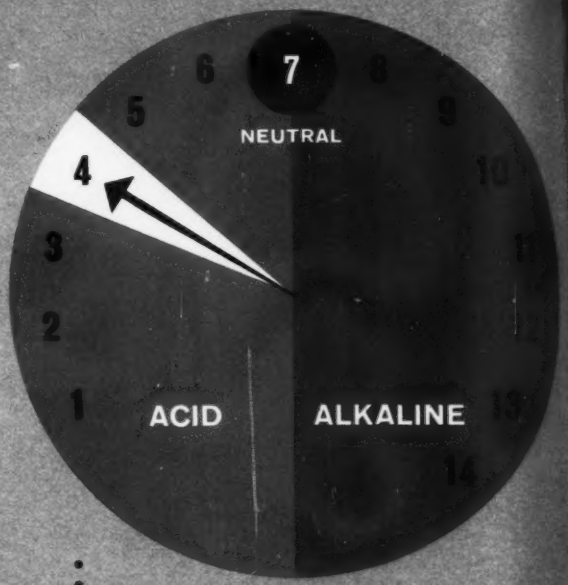
Valuable adjunct in management of monilia, trichomonas, staphylococcus and streptococcus vaginal infections.

*See reverse side for detail.

MASSENGILL® POWDER

THE [illegible] MASSENGILL COMPANY
[illegible] City

pH



massengill® powder

The **BUFFERED**
acid vaginal douche

What is a BUFFER?

Medical dictionaries define it as a substance which, added to a solution, causes resistance to any change of hydrogen-ion concentration (pH) when either acid or alkali is added.

Significance of buffers in Massengill Powder

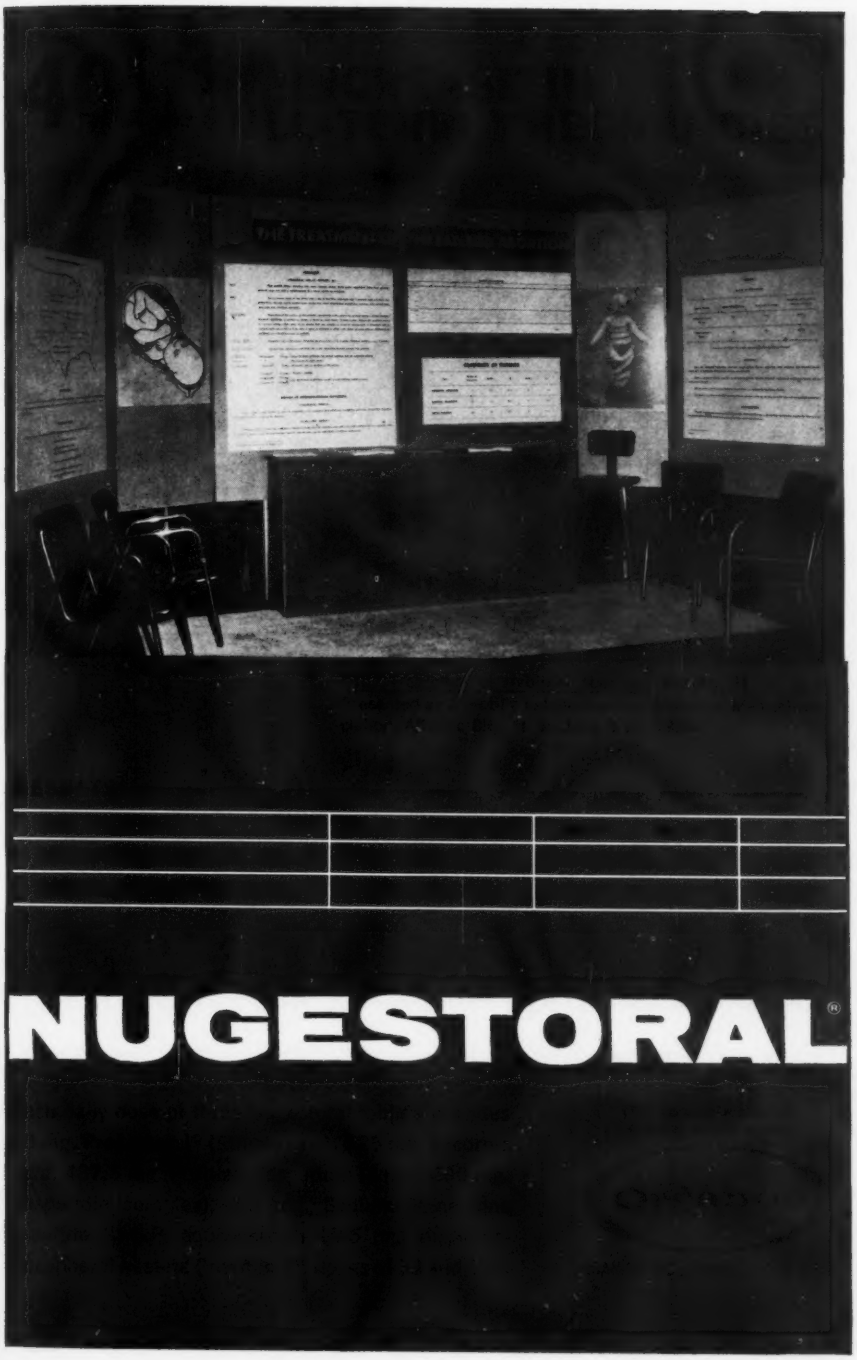
The normal vagina has a pH of 3 to 4.5. This low pH inhibits growth of most pathogenic invaders. Usually, an infection will cause the pH to rise to the neutral or alkaline range which favors the multiplication of pathogens.

The alkaline mucosa neutralizes a simple, unbuffered acid douche, like vinegar, within 30 minutes.

In contrast, the *buffered* acid douche solution of Massengill Powder (pH 3.5–4.5) resists neutralizing. The normal, low pH is maintained for 4 to 6 hours and as long as 24 hours in recumbent patients. This low pH inhibits the propagation of monilia, trichomonas vaginalis and pathogenic bacteria. However, the beneficial Döderlein bacillus thrives in this pH range.

THE S. E. MASSENGILL COMPANY

Bristol, Tennessee • New York • Kansas City • San Francisco


NUGESTORAL®

In the menopause...
transition without tears

Milprem promptly relieves emotional distress with lasting control of physical symptoms

Milprem®

Miltown®+conjugated estrogens (equine)

Supplied in two potencies for dosage flexibility:

MILPREM-400, each coated pink tablet contains 400 mg. Miltown (meprobamate) and 0.4 mg. conjugated estrogens (equine).

MILPREM-200, each coated old-rose tablet contains 200 mg. Miltown and 0.4 mg. conjugated estrogens (equine).

Both potencies in bottles of 60.

Literature and samples on request.

In minutes, Milprem starts to ease anxiety and depression. It relieves insomnia, relaxes tense muscles; alleviates low back pain and tension headache. As the patient continues on Milprem, the replacement of estrogens checks hot flushes and other physical symptoms.

Easy dosage schedule: One Milprem tablet t.i.d. in 21-day courses with one-week rest periods; during the rest periods, Miltown alone can sustain the patient.

WALLACE LABORATORIES, *New Brunswick, N. J.*

CHP-9224-59

for
vaginal
douching
that is
physiologically
sound

ethically promoted

Meta Cine

vaginal douche powder

Meta Cine represents a carefully designed formula which provides the physician with a vaginal douche preparation which safely and effectively maintains a clean healthy vagina.

Meta Cine is a combination of several ingredients clinically established as valuable in promoting proper vaginal hygiene. Diluted for use, Meta Cine possesses the desired pH (3.5); contains the mucus digestant, papain, which dissolves mucus plugs and coagulum; contains lactose to promote growth of desirable döderlein bacilli, and methyl salicylate for soothing stimulation of circulation within the vaginal walls.

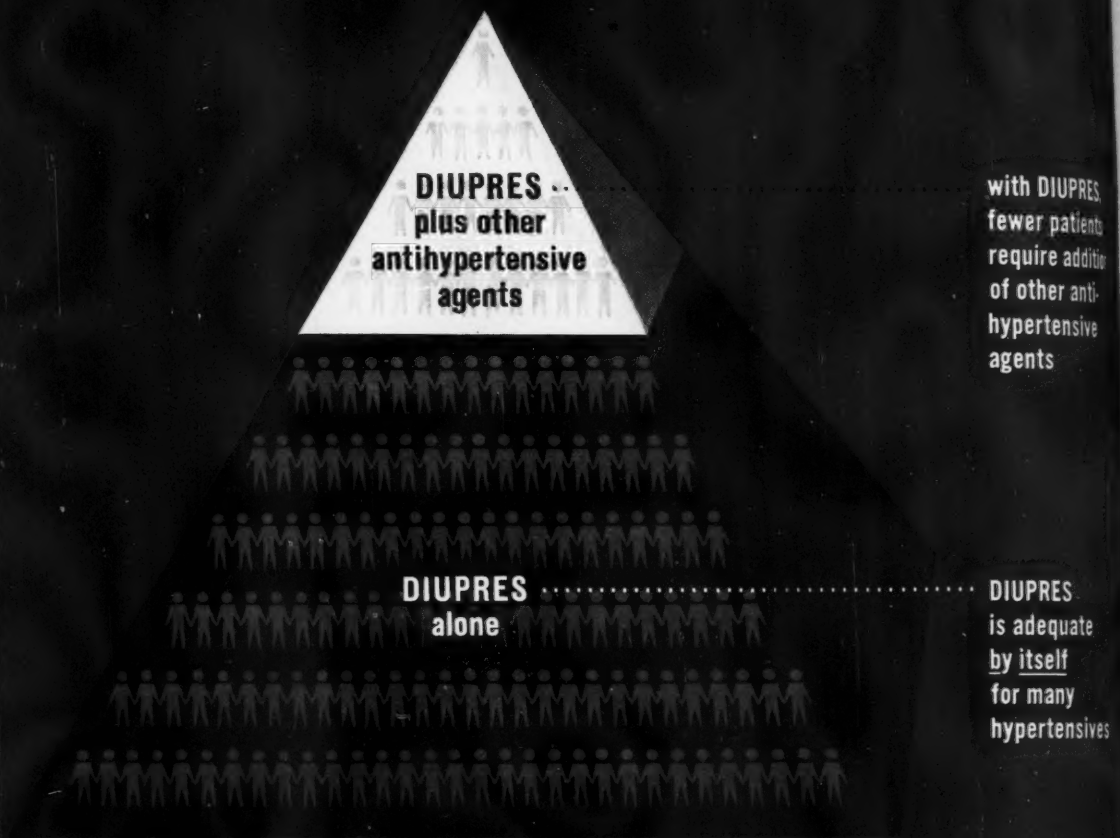
Its pleasant, deodorizing fragrance also meets the esthetic demands of your patients.

Meta Cine is promoted exclusively to the medical profession, and recommends itself as your preparation of choice for patients who might otherwise indulge in unsupervised self-medication with potentially damaging nonphysiologic douches.

Supplied in 8-oz. containers, and boxes of 30 individual-dose packettes. Two teaspoonfuls, or contents of one packette, in 2 quarts of warm water, douche as prescribed.

Printed douching instructions for patients available upon request

BRAYTEN Pharmaceutical Company • *Chattanooga 9, Tennessee*



DIUPRES PROVIDES "BROAD-BASE" ANTIHYPERTENSIVE THERAPY

...is effective by itself in a majority of patients with mild or moderate hypertension, and even in many with severe hypertension

greatly improved and simplified management of hypertension

DIUPRES*

DIURIL® WITH RESERPINE

the first "wide-range" antihypertensive—effective in mild, moderate, and severe hypertension

- more hypertensives can be better controlled with **DIUPRES** alone than with any other agent . . . with greater simplicity and convenience, and with decreased side effects
- can be used as total therapy or primary therapy, adding other drugs if necessary
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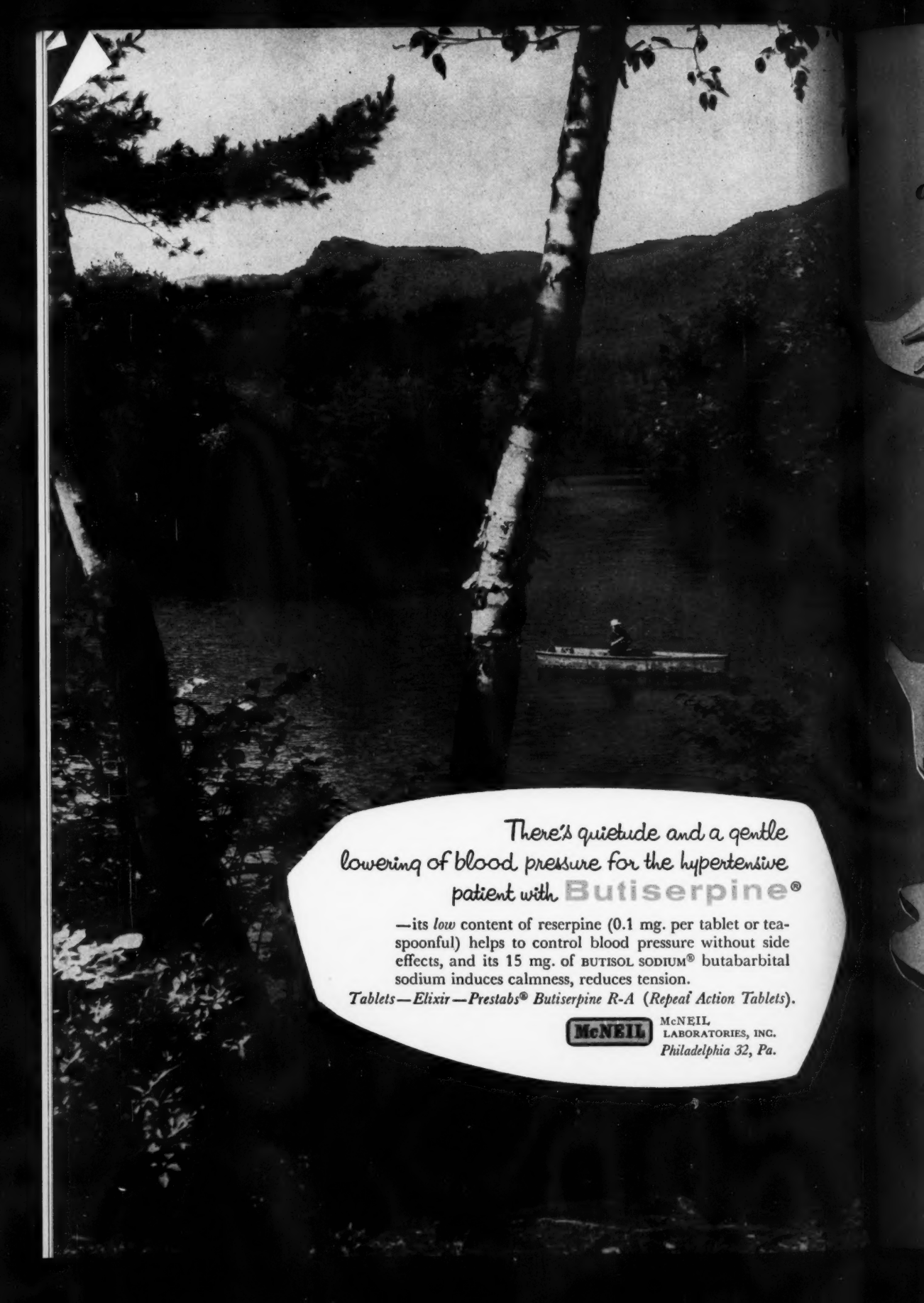
- should other drugs need to be added, they can be given in much lower than usual dosage so that their side effects are often strikingly reduced
- organic changes of hypertension may be arrested and reversed . . . even anginal pain may be eliminated
- patient takes one tablet rather than two . . . dosage schedule is easy to follow
- economical

DIUPRES-500 500 mg. DIURIL (chlorothiazide), 0.125 mg. reserpine. One tablet one to three times a day.

DIUPRES-250 250 mg. DIURIL (chlorothiazide), 0.125 mg. reserpine. One tablet one to four times a day.

MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., PHILADELPHIA 1, PA.

*DIUPRES AND DIURIL (CHLOROTHIAZIDE) ARE TRADEMARKS OF MERCK & CO., INC.


There's quietude and a gentle lowering of blood pressure for the hypertensive patient with Butiserpine®
—its *low* content of reserpine (0.1 mg. per tablet or teaspoonful) helps to control blood pressure without side effects, and its 15 mg. of BUTISOL SODIUM® butabarbital sodium induces calmness, reduces tension.
Tablets—Elixir—Prestabs® Butiserpine R-A (Repeat Action Tablets).
McNEIL
McNEIL LABORATORIES, INC.
Philadelphia 32, Pa.

When the illness is not acute and the diagnosis is not obvious

Rx *A clarifying prescription*

solfoton

Will relieve symptoms due to emotional stress — and leave unchanged those symptoms due to organic pathology.

Issued in tablet or capsule form

EACH TABLET OR CAPSULE CONTAINS:

PHENOBARBITAL . . . . . ¼ grain
Warning: may be habit-forming

SULFUR, COLLOIDAL . . . . . ½ grain

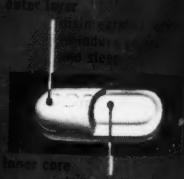
DOSAGE: One, three or four times a day for at least two weeks.

Wm. P. Poythress *& Co., Inc.*

RICHMOND 17, VIRGINIA

For those patients who complai bou

carries your patients through the middle of the night



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Each Nebralin timed-release tablet contains:

Dorsthal® .....

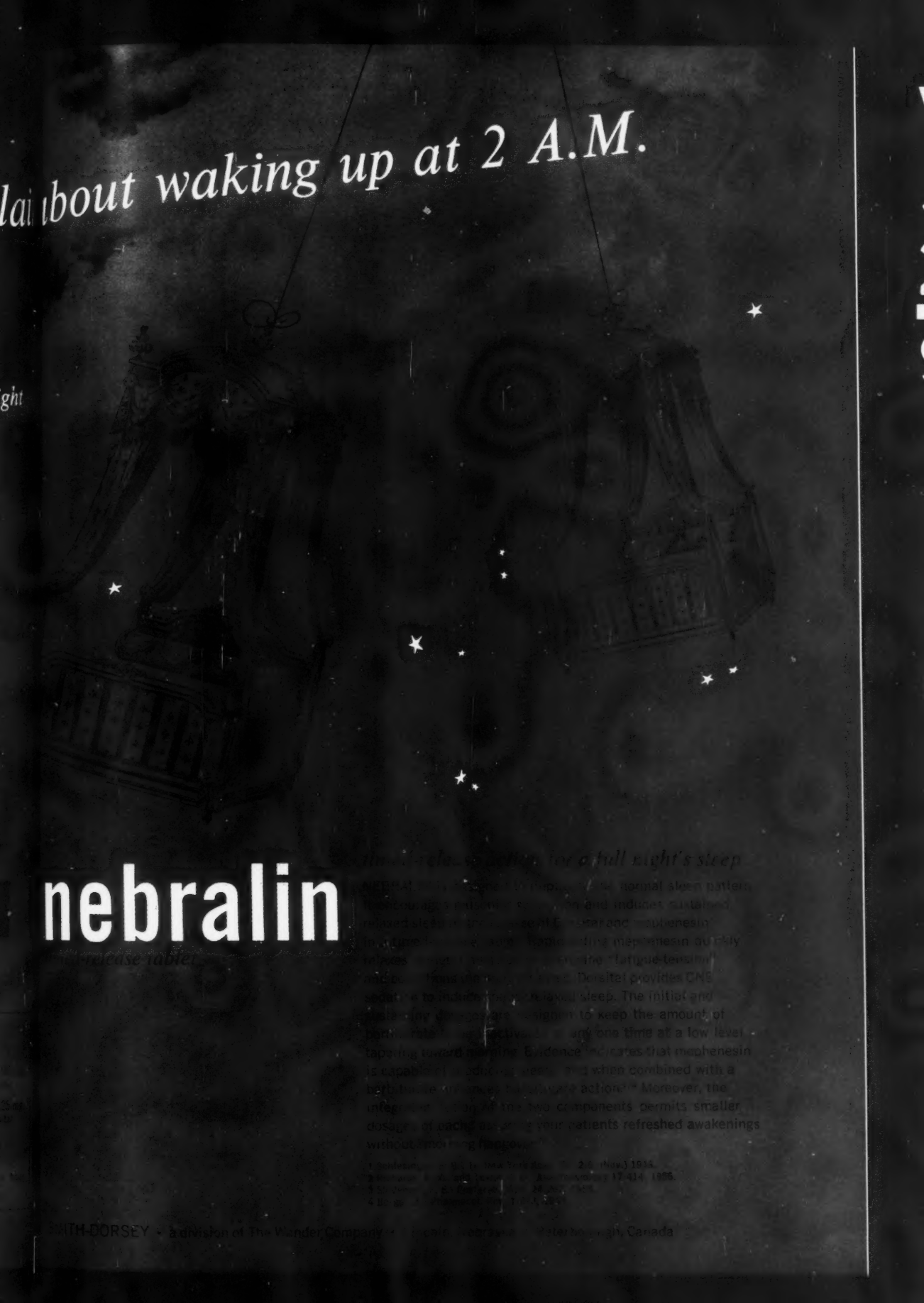
Warning: May be habit forming

Mephenesin 2

®Dorsey brand of pentobarbital

CAUTION: Federal law prohibits dispensing without prescription

Dosage: One or two tablets at bedtime before retiring.


laibout waking up at 2 A.M.
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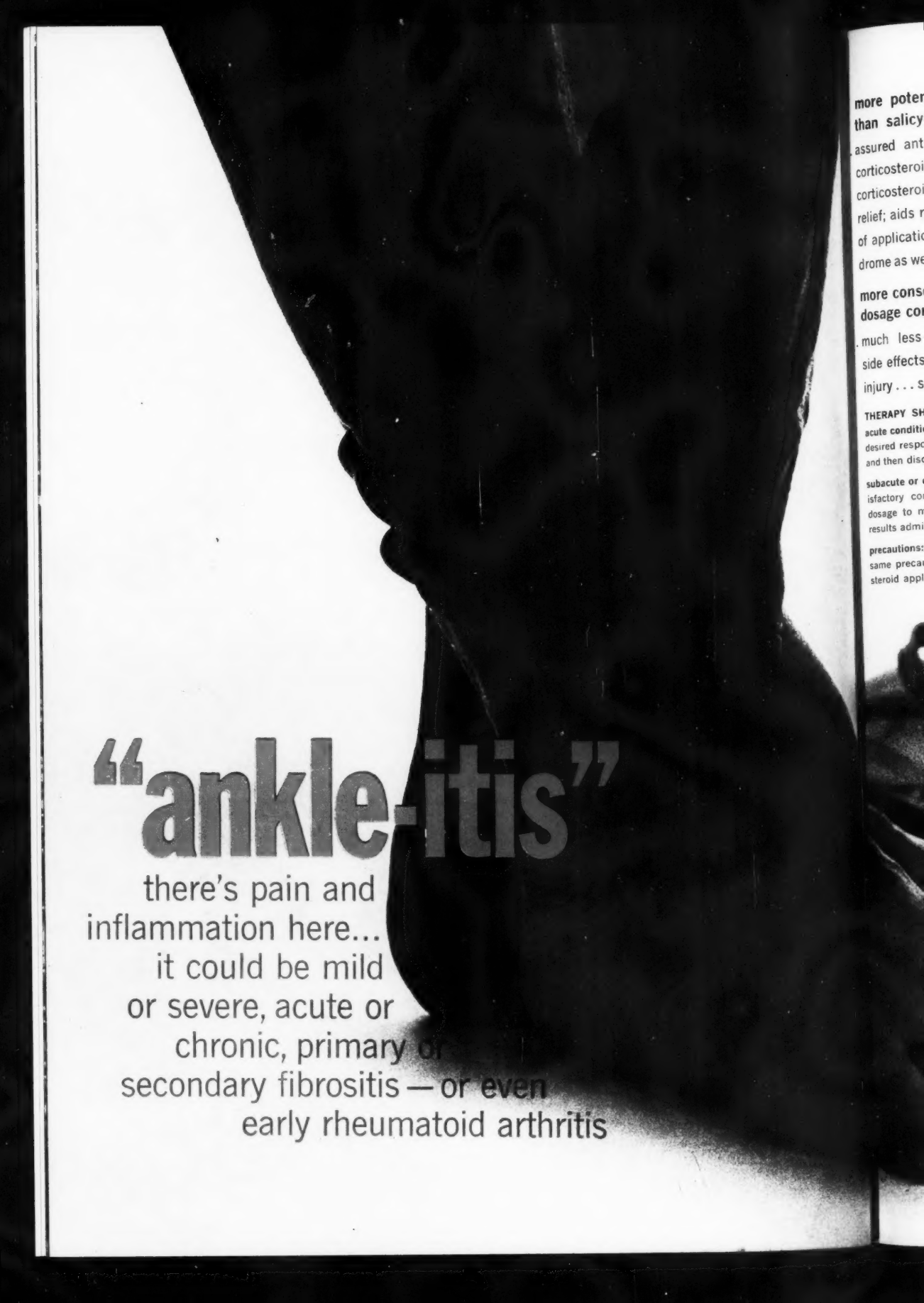
"ankle-itis"
there's pain and inflammation here... it could be mild or severe, acute or chronic, primary or secondary fibrositis — or even early rheumatoid arthritis

more potent and comprehensive treatment than salicylate alone

assured anti-inflammatory effect of low-dosage corticosteroid[1] . . . additive antirheumatic action of corticosteroid plus salicylate[2-5] brings rapid pain relief; aids restoration of function . . . wide range of application including the entire fibrositis syndrome as well as early or mild rheumatoid arthritis

more conservative and manageable than full-dosage corticosteroid therapy—

much less likelihood of treatment-interrupting side effects[1-6] . . . reduces possibility of residual injury . . . simple, flexible dosage schedule

THERAPY SHOULD BE INDIVIDUALIZED

acute conditions: Two or three tablets four times daily. After desired response is obtained, gradually reduce daily dosage and then discontinue.

subacute or chronic conditions: Initially as above. When satisfactory control is obtained, gradually reduce the daily dosage to minimum effective maintenance level. For best results administer after meals and at bedtime.

precautions: Because SIGMAGEN contains prednisone, the same precautions and contraindications observed with this steroid apply also to the use of SIGMAGEN.

in any case it calls for

Sigmagen®

corticoid-salicylate compound tablets

Composition

METICORTEN® (prednisone)	0.75 mg.
Acetylsalicylic acid	325 mg.
Aluminum hydroxide	75 mg.
Ascorbic acid	20 mg.

Packaging: SIGMAGEN Tablets, bottles of 100 and 1000.

References: 1. Spies, T. D., et al.: J.A.M.A. 159:645, 1955. 2. Spies, T. D., et al.: Postgrad. Med. 17:1, 1955. 3. Gelli, G., and Della Santa, L.: Minerva Pediat. 7:1456, 1955. 4. Guerra, F.: Fed. Proc. 12:326, 1953. 5. Busse, E. A.: Clin. Med. 2:1105, 1955. 6. Sticker, R. B.: Panel Discussion, Ohio State M. J. 52:1037, 1956.

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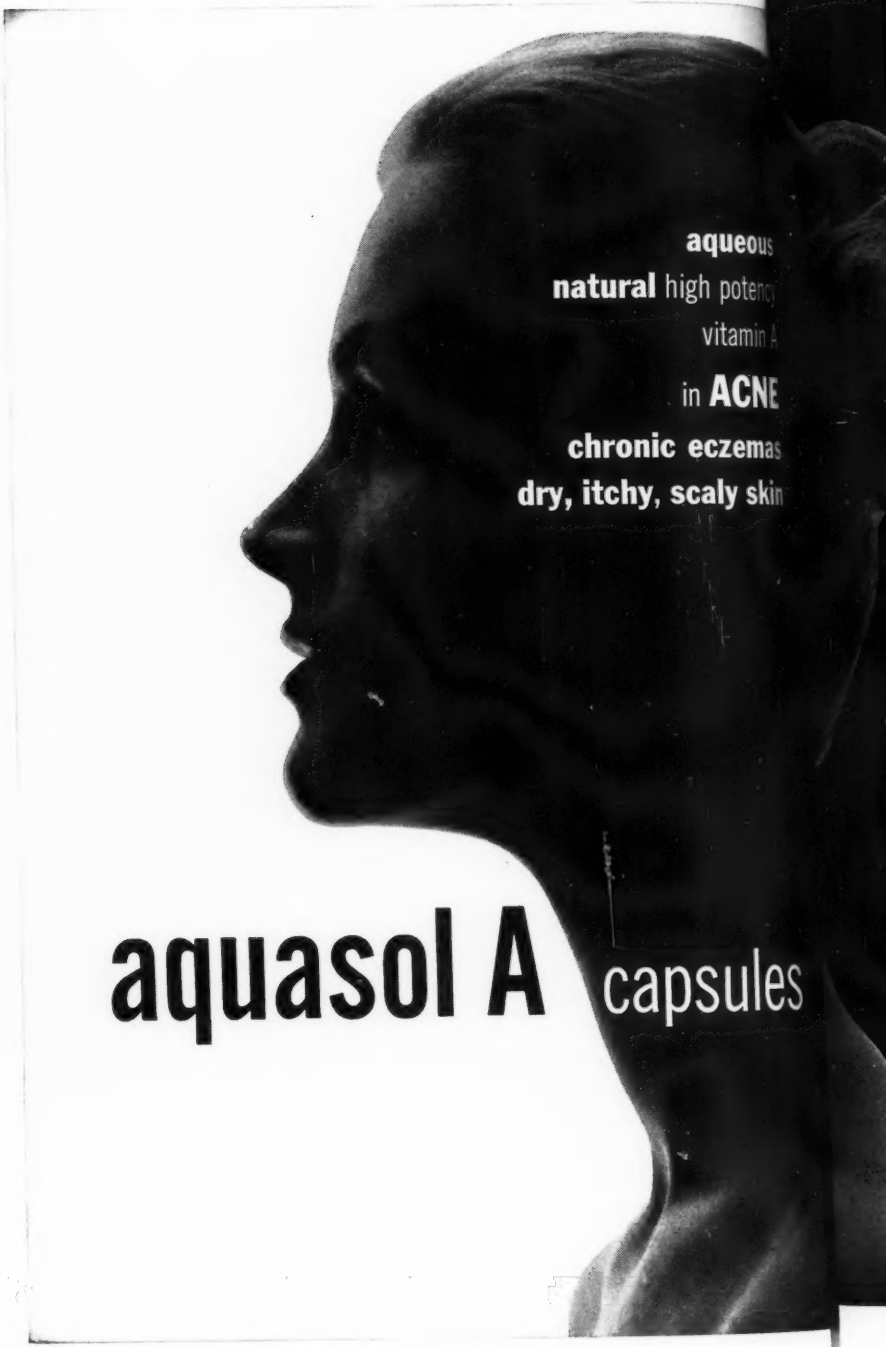
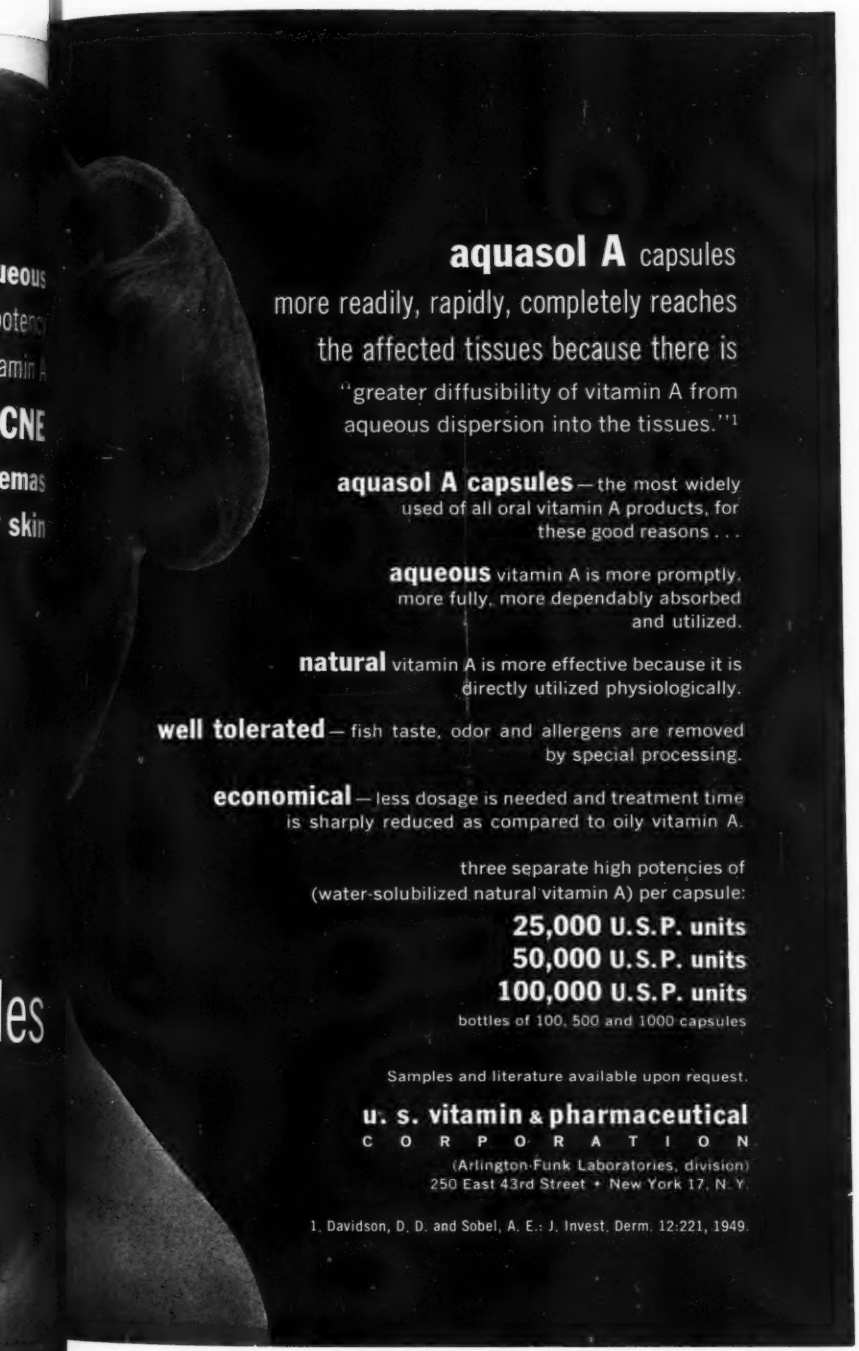

aqueous
natural high potency
vitamin A
in ACNE
chronic eczemas
dry, itchy, scaly skin
aquasol A capsules



aquasol A capsules
more readily, rapidly, completely reaches
the affected tissues because there is
"greater diffusibility of vitamin A from
aqueous dispersion into the tissues."[1]

aquasol A capsules—the most widely used of all oral vitamin A products, for these good reasons . . .

aqueous vitamin A is more promptly, more fully, more dependably absorbed and utilized.

natural vitamin A is more effective because it is directly utilized physiologically.

well tolerated—fish taste, odor and allergens are removed by special processing.

economical—less dosage is needed and treatment time is sharply reduced as compared to oily vitamin A.

three separate high potencies of
(water-solubilized natural vitamin A) per capsule:

25,000 U.S.P. units
50,000 U.S.P. units
100,000 U.S.P. units
bottles of 100, 500 and 1000 capsules

Samples and literature available upon request.

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C O R P O R A T I O N
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250 East 43rd Street • New York 17, N. Y.

1. Davidson, D. D. and Sobel, A. E.: J. Invest. Derm. 12:221, 1949.

when the
rheumatic
disorder
is more
than salicylates
alone
can control...

MORE
HIGHLY INDIVIDUALIZED
THERAPY
FOR THE
RHEUMATIC
"IN-BETWEEN"

...
con
requires
th
ster
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Aristo

wider latitude in adjusting dosage

ARISTOGESIC is particularly effective for relief of chronic – but less severe – pain of rheumatic origin. ARISTOGESIC combines the anti-inflammatory effects of ARISTOCORT® Triamcinolone with the analgesic action of salicylamide, a highly potent salicylate. Dosage requirements for ARISTOGESIC are substantially lower than generally required for each agent alone. The exceptionally wide latitude of dosage adjustment with ARISTOGESIC permits well-tolerated therapy for long periods of time with fewer side effects.

Indications: Mild cases of rheumatoid arthritis, tenosynovitis, synovitis, bursitis, mild spondylitis, myositis, fibrositis, neuritis, and certain muscular strains.

Dosage: Average initial dosage: 2 capsules 3 or 4 times daily. Maintenance dosage to be adjusted according to response.

Precautions: All precautions and contraindications traditional to corticosteroid therapy should be observed. The amount of drug used should be carefully adjusted to the lowest dosage which will suppress symptoms. Discontinuance of therapy must be carried out gradually after patients have been on steroids for prolonged periods.

Each ARISTOGESIC Capsule contains:

ARISTOCORT® Triamcinolone	0.5 mg.
Salicylamide	325 mg.
Dried Aluminum Hydroxide Gel	75 mg.
Ascorbic Acid	20 mg.

Supply: Bottles of 100 and 1,000.

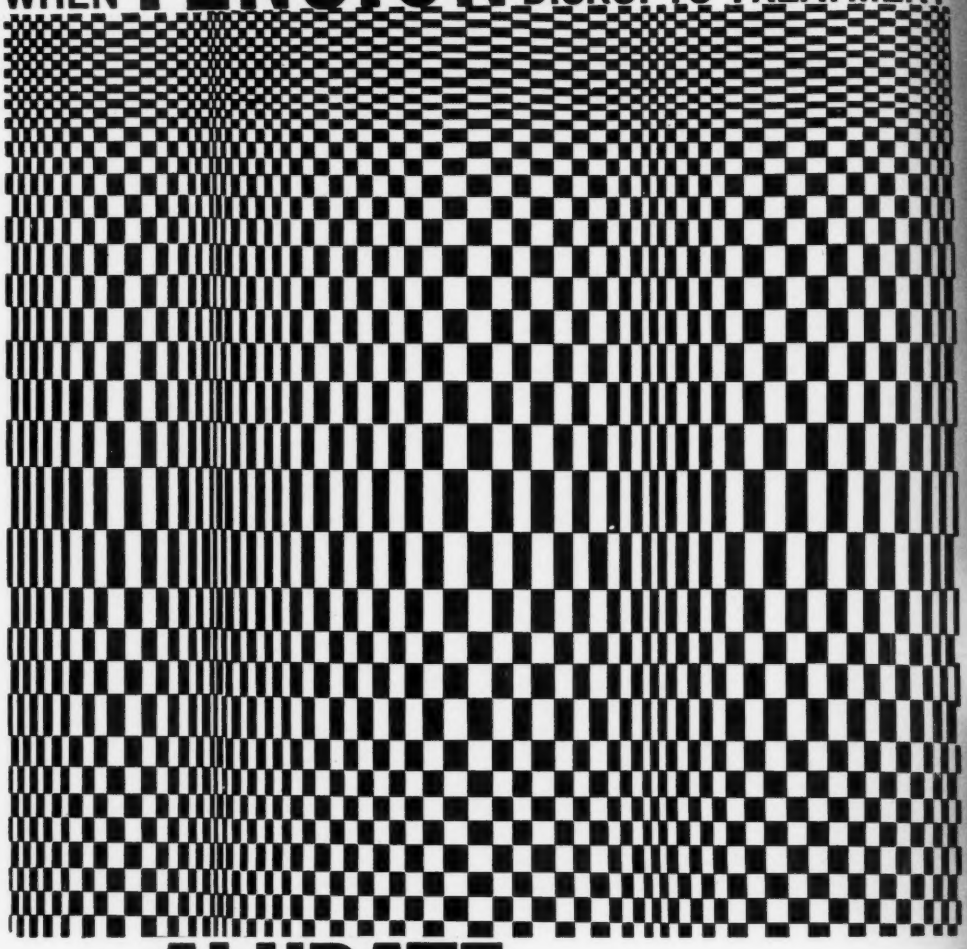
gesic® Capsules

Steroid-Analgesic Compound LEDERLE

Lederle

ERLE LABORATORIES, A Division of AMERICAN CYANAMID COMPANY, Pearl River, New York

WHEN TENSION DISRUPTS TREATMENT



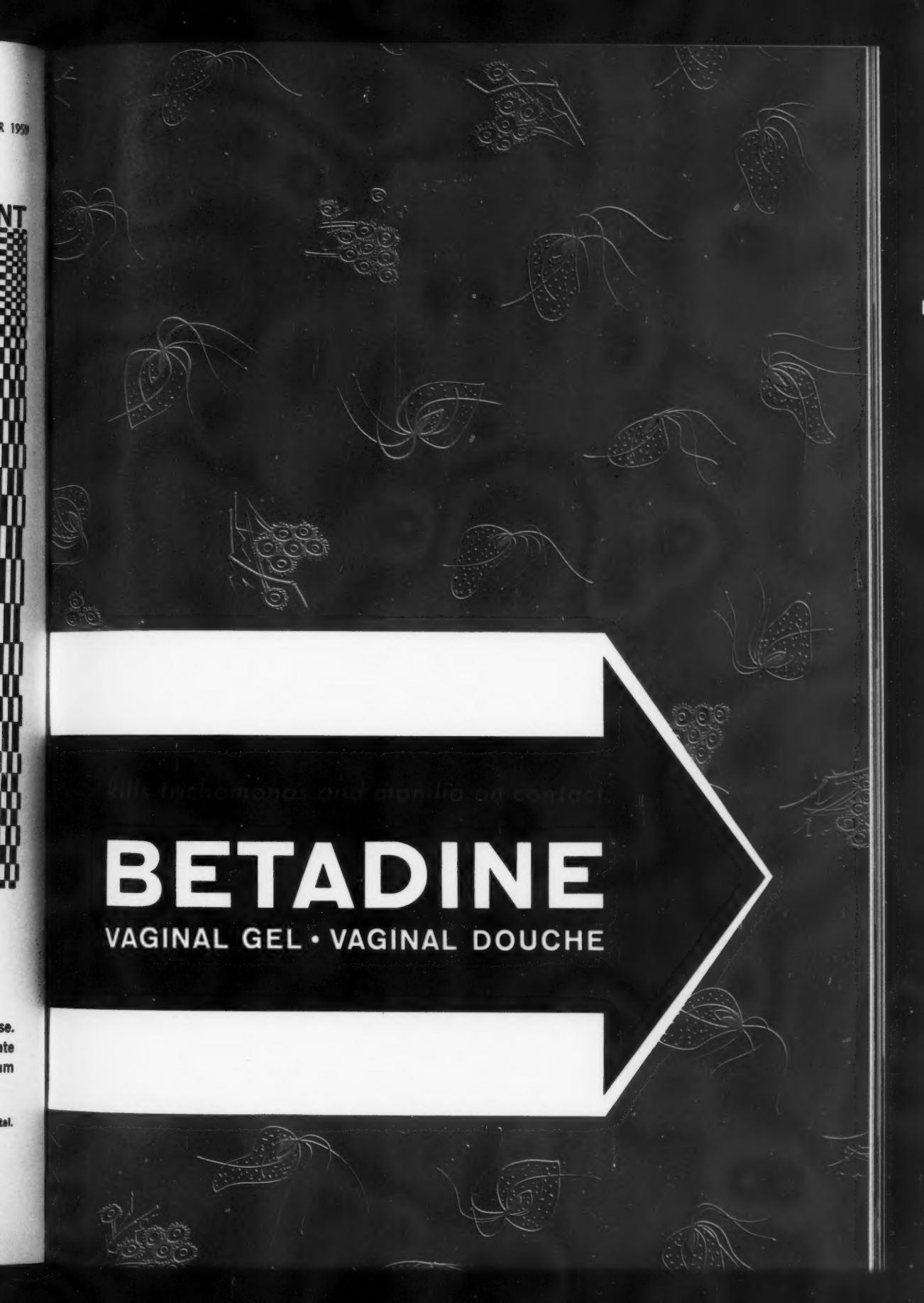
ELIXIR ALURATE DISRUPTS TENSION

Dependable, prompt-acting daytime sedative.

Broad margin of safety. Virtually no drowsiness. Over a quarter century of successful clinical use. Alurate is effective by itself and compatible with a wide range of other drugs. To avoid barbiturate identification or abuse, Alurate is available as Elixir Alurate (cherry-red) and Elixir Alurate Verdum (emerald-green).

Adults: ½ to 1 teaspoonful of either Elixir Alurate or Elixir Alurate Verdum, 3 times daily. ALURATE®—brand of aprobarbital.

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc • Nutley 10, N. J.


Kills trichomonas and candida on contact.
BETADINE
VAGINAL GEL • VAGINAL DOUCHE

BETADINE

brand of Povidone-Iodine, possesses broad-range germicidal activity against fungi, yeasts, bacteria, protozoa, and viruses. In the vaginal tract Betadine Vaginal Gel and Betadine Vaginal Douche kill trichomonas and monilia on contact and destroy common pathogens. Betadine is virtually nonirritating to vaginal mucosa.

indicated:

in the treatment of trichomoniasis, moniliasis and nonspecific vaginitis.

advantages:

- almost immediate relief from leukorrhea, pruritus; diminishes malodor
- unsurpassed broad-range microbicidal activity
- therapeutically active even in the presence of blood, pus, vaginal secretions
- wetting action to assist penetration into vaginal crypts and crevices

how to use:

In the office: Swab the vaginal vault with Betadine Antiseptic, full strength.

prescribe Betadine Vaginal Douche for therapeutic use as follows: Two (2) tablespoonfuls to a quart of lukewarm water once daily by the patient at home, for six days. On the seventh day, the patient returns for re-examination and swabbing with Betadine Antiseptic; an additional week of therapeutic douching if necessary.

prescribe Betadine Vaginal Gel as follows: Insert one (1) applicatorful of Betadine Vaginal Gel each night, followed by a douche the next morning, through the entire menstrual cycle. If further therapy is warranted, the gel should be continued only during the actual menses days of the following two menstrual periods.

After the infection has been brought under control, the use of Betadine Vaginal Douche is recommended twice weekly at a dilution of one (1) tablespoonful to a quart of lukewarm water.

established in 1905

TAILBY-NASON COMPANY, INC., Dover, Delaware

BETADINE® VAGINAL GEL

3 OZ. TUBE WITH APPLICATOR

BETADINE® VAGINAL DOUCHE

8 OZ. BOTTLE

MEDIEVAL TORTURE CHAMBER
THE BETTMANN ARCHIVE

Free the anemic from iron intolerance...

For Efficient Prophylaxis and Predictable Therapeutic Response without Gastric Irritation
—in iron deficiency, pernicious and other macrocytic anemias*

FOR BETTER, QUICKER RESPONSE IN THERAPEUTICS OR PROPHYLAXIS AND TO ENSURE PROPER MAINTENANCE—PRESCRIBE

FERGON PLUS
CAPLETS

2 Caplets contain:

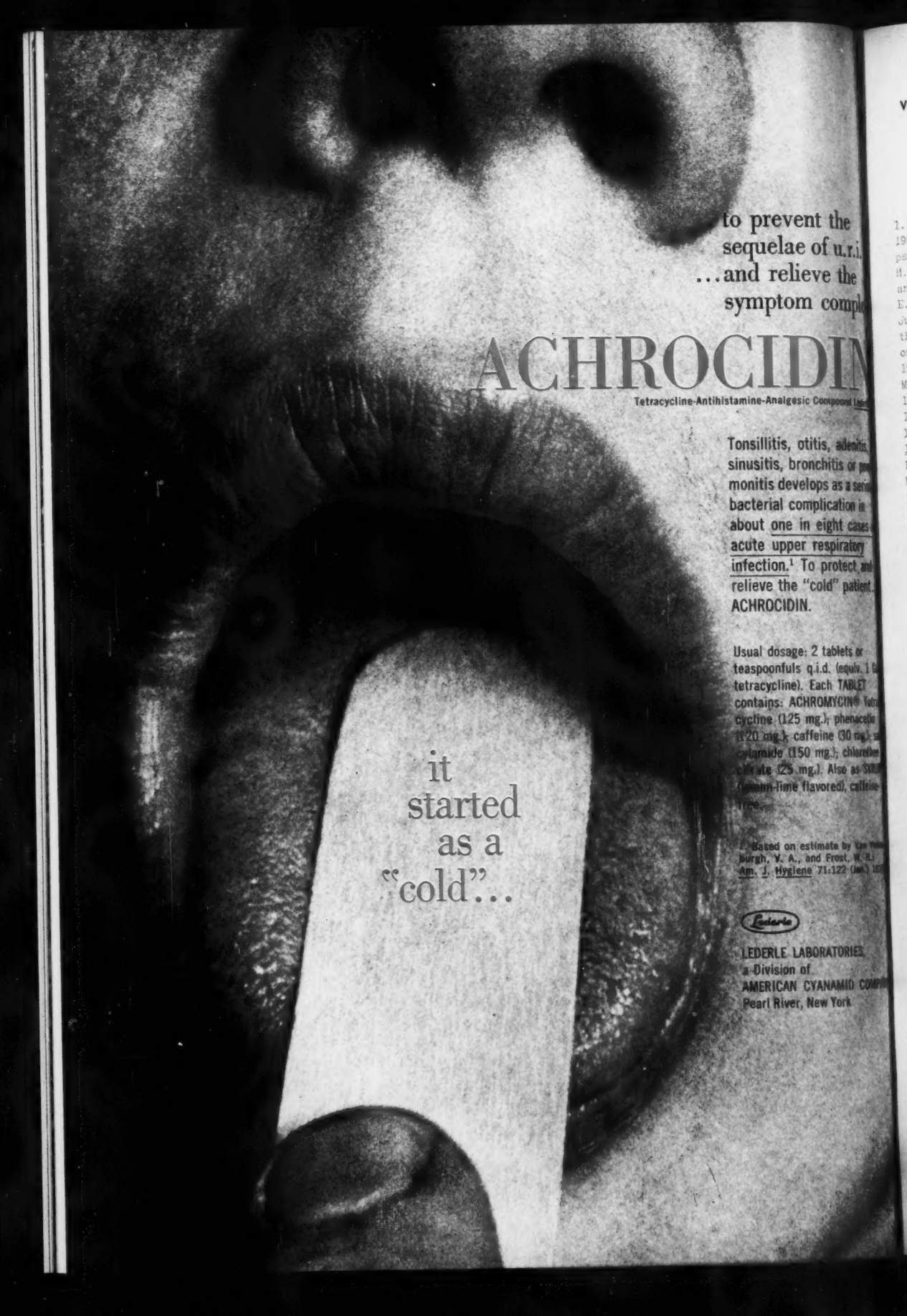
Fergon (brand of ferrous gluconate) *iron without irritation*	1000 mg.
Vitamin B_{12} with Intrinsic Factor Concentrate U.S.P.	1 unit (oral)
Folic acid	3 mg.
Ascorbic acid	150 mg.

Therapeutic dose:
Only 2 Fergon Plus Caplets daily (one before the morning and evening meals).

Bottles of 100 and 500.

*Seriously ill patients, particularly those with neurologic symptoms, also need parenteral therapy.

Winthrop LABORATORIES
New York 18, N. Y.



to prevent the
sequelae of u.r.i.
...and relieve the
symptom comple

ACHROCIDIN

Tetracycline-Antihistamine-Analgesic Compound Le

Tonsillitis, otitis, adenitis, sinusitis, bronchitis or pn monitis develops as a seri bacterial complication in about one in eight cases acute upper respiratory infection.[1] To protect and relieve the "cold" patient, ACHROCIDIN.

Usual dosage: 2 tablets or teaspoonfuls q.i.d. (equiv. 1 g tetracycline). Each TABLET contains: ACHROMYCIN® Tetra cycline (125 mg.); phenacetin (120 mg.); caffeine (30 mg.); sulfacetamide (150 mg.); chlorcyclizine citrate (25 mg.). Also as SYRUP (lemon-lime flavored), caffeine-free.

1. Based on estimate by Van Vleet, Pittsburgh, V. A., and Frost, W. H.: Am. J. Hygiene 71:122 (Jan.) 1960.

Lederle

LEDERLE LABORATORIES
a Division of
AMERICAN CYANAMID COMPANY
Pearl River, New York

1. Borrus, J. C.: J.A.M.A. 157:15[illegible] 30, 1[illegible] 2. Sell[illegible] S.: J.A.M.A. 157:1594, April 30, 1955. 3. Lemere, F.: [illegible]thwest Med[illegible] 98, Oct. [illegible]5. 4. Bene[illegible] B. and M[illegible]cutti, C.: Lav. neuropsichiat. 18:693, J[illegible]6. Sellin[illegible]: J. Clin [illegible] Exper. Psy[illegible]h. 17:7[illegible] March 1956. 6. Berglund, M., Blumenthal, B[illegible]lordh, P.: [illegible]ska läk. 5[illegible]3362, Dec. [illegible]1956. 7. [illegible]l, H. A., Wood, J. A. and Dixon, H. H.: [illegible]w York Acad[illegible]c. 67:780, May 9, 1957. 8. Hollister[illegible], L., Elkins, H., Hiler, E. G. and St. Pierr[illegible] Ann. New Yo[illegible] Acad. Sc. 67:789, May 9, [illegible]57. 9. G[illegible]: Rass. med. 34:233, July-Aug[illegible]57. 10[illegible]4, R. et al.: J. Pediat. P[illegible]is 20:27, [illegible]6. 1957. [illegible]iklund, P[illegible]: Anaesthesist [illegible]7, Aug[illegible]7. 12. Tucker, W. I.: Sout[illegible] J. 50:1111, Sept. 195[illegible]5. Rolandi[illegible] Attual. ostet. [illegible]3(6)[illegible]9, Nov.-Dec. 1957. 14. [illegible]ecker, W.: Klin. Mon[illegible]. J. Augenh[illegible]):224, 1958. [illegible]bianco[illegible]. and Cer[illegible]i, T.: Oto-r[illegible]ng. ital. 28(2):143, 1958. 16. [illegible], G.: Miner[illegible]9:1914, 1958. 17. [illegible]uso, R. and [illegible]i, F.: Ac[illegible]eurol. [illegible]3(1):36, J[illegible]1958. 18. [illegible]Gazz. med. ital.[illegible]49, Feb. 1[illegible]5[illegible]stur, R.[illegible] J. Indian M. Prof[illegible]3, Feb. 1958. [illegible]t, W.: Therap.[illegible]97:66, Fe[illegible]21. B[illegible]: Lyon méd. 19[illegible] March 2, 1958. [illegible]iglia, G.: Mine[illegible]10:218, M[illegible]15, 1958. [illegible]lander, H. S.: [illegible] Cardiol. 1:395, [illegible] 1958. 24. McCle[illegible] Arch. Pea[illegible]75:101, [illegible]25. Sprauer, V[illegible] J. Internat. Rec. Med. [illegible] GP Clinics 171:[illegible] 1958. 26. [illegible]binson, R.[illegible]obinson, H. M., [illegible]r.: South. M. J. 51:609, April 1958. 27. [illegible] S. and Pe[illegible]er, L.: N[illegible]ed. 58:1285, April 15, 1958. 28. Bouquerel, J., Naviau and [illegible]e: Ann. méd. [illegible]ychol. 116[illegible]e 1958. 29. Reboul, E., Reboul, M. and Dorgeuille, C.: Maroc [illegible]7:784, July 1958. 30. B[illegible] Lyon méd. 200:885, Nov. 1958. 31. Lamphier, T. A.: Maryland M[illegible]7:627, Nov. 1958. 32. Leuke[illegible] Med. Klin. 53:2113, Dec. 1958.

70-95%

of nervous, tense patients recovered or improved

For your patients, Miltown promptly checks emotional and muscular tension. Thus, you will make it easier for them to lead a normal family life and to carry on their usual work.

For you, the choice of Miltown as the tranquilizer means the comfortable assurance that it will relieve nervousness and tension without impairing your patient's mental efficiency, motor control, normal behavior or autonomic balance.

meprobamate (Wallace)

Miltown®

Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; bottles of 50

WALLACE LABORATORIES, *New Brunswick, N. J.*

CM-8304

what to do about RUNS...
eye RUNS...
nose RUNS...

patient "blue" and listless

in allergy

NALERTAN

a new Neisler Durabond® product

dries secretions

eliminates congestion

stops itching

brightens the outlook

all day or night with a single oral dose . . . with a remarkable lack of side effects

in pollen allergies, contact dermatoses, food sensitivities, and a wide variety of allergic associated disorders

NALERTAN provides

new chemical forms of two outstanding antihistamines . . . acting synergistically for broad, prolonged blockage of histamine response.

a long-acting sympathomimetic . . . to lift the misery, combat lassitude and brighten the outlook . . . hasten recovery.

Employs the Durabond principle . . . to act within minutes . . . relieves for hours . . . Just one dose in the morning controls lacrimation, makes breathing easier, relieves itching—all day. And, one dose upon retiring keeps the patient symptom-free . . . allows uninterrupted rest all night.

1 or 2 tablets twice a day. For economy, prescribe in original pkgs. of 100.

Each Durabond tabule contains: Chlorpheniramine tannate, 8 mg.; Pyrilamine tannate, 25 mg.; Tanphetamin (*d*-amphetamine tannate), 10 mg.

Neisler **IRWIN, NEISLER & CO.**
DECATUR, ILLINOIS

A LESS "STORMY" COURSE FOR SOME POORLY CONTROLLED DIABETICS THANKS TO DIABINESE®

brand of chlorpropamide

tablets / once-a-day dosage

"...has proved to be extremely useful in improving the control of the patient who has been uncontrolled on other regimens."[1]

The specific pharmacologic properties of DIABINESE—high activity, freedom from metabolic degradation, and gradual excretion—permit (1) prompt lowering of elevated blood sugar levels *without a "loading" dose*, and (2) smooth, sustained maintenance "devoid of...marked blood sugar fluctuations"[2] on convenient, lower-cost, once-a-day dosage. This is the consensus of extensive clinical literature.[1-11] Widespread use of DIABINESE since its introduction has confirmed the low incidence of side effects reported by the original investigators.

Thus, DIABINESE merits *first* consideration for any diabetic presently receiving or potentially better managed with oral therapy—including many diabetics for whom previous oral agents have proved ineffective.

Supplied: Tablets, white, scored 250 mg., bottles of 60 and 250; 100 mg., bottles of 100.

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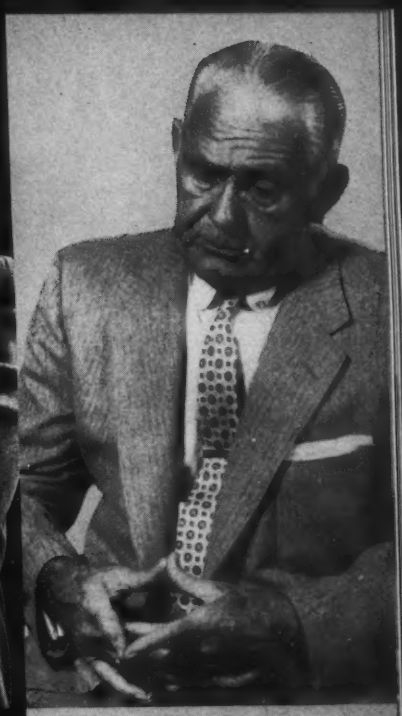
1. Dobson, H., et al.: Ann. New York Acad. Sc. 74:940, 1959. 2. Greenhouse, B.: Ibid., p. 643. 3. Forsham, P. H.; Magid, G. J., and Dorosin, D. E.: Ibid., p. 672. 4. Beaser, S. B.: Ibid., p. 701; New England J. Med. 259:573, 1958. 5. Bloch, J., and Lenhardt, A.: Ann. New York Acad. Sc. 74:954, 1959. 6. O'Driscoll, B. J.: Lancet 2:749, 1958. 7 Hadley, W. B.; Khachadurian, A., and Marble, A.: Ann. New York Acad. Sc. 74:621, 1959. 8. Duncan G. G.; Schless, G. L., and Deweshkieh, M. M. A.: Ibid., p. 717. 9. Handelsman, M. B.; Levitt. L., and Celebretta, M. F.: Ibid., p. 632. 10. Hills, A. G., and Abelove, W. A.: Ibid., p. 843. 11. Drey, N. W., et al.: Ibid., p. 962.

in anxiety and tension your patient can meet the rigors of life

He's... active alert



not... lethargic inattentive

BUTISOL *sodium*®

butabarbital sodium

Jitteriness, apprehension, nervousness and the enervating insomnia which characterize the "anxiety state" encountered in daily practice are easily controlled by small, daytime Butisol® dosage.

As shown recently[1] in a prolonged comparative study of routine anxiety patients, Butisol "was found to be the most effective sedative which will produce satisfactory daytime sedation...with minimal occurrence of untoward reactions. Large nighttime hypnotic doses are unnecessary in the majority of patients."[2]

1. Batterman, R. C.; Grossman, A. J.; Mouratoff, G. J., and Leifer, P.: A Clinical Re-evaluation of Daytime Sedatives, Scientific Exhibit, Annual Meeting of AMA, San Francisco, June 23-27, 1958.

2. Grossman, A. J.; Batterman, R. C., and Leifer, P.: Fed. Proc. *17*:373 (March) 1958.

BUTISOL sodium® TABLETS • REPEAT-ACTION TABLETS • ELIXIR • CAPSULES

McNEIL LABORATORIES, INC. • PHILADELPHIA 32, PA.

McNEIL

"EXCELLENT,"[3]

"MARKED,"[1]

"PRONOUNCED,"[2]

"SIGNIFICANT"[4] or

"GRATIFYING"[5]

results in 80.3% of cases of acute skeletal muscle spasm, and "moderate" results in 14.1%—or an over-all beneficial result in 94.4% of cases. Relatively free of adverse side effects.[1,2,4,5]

Now—in acute skeletal muscle spa

A SPEEDIER RETURN T

1 **In 33 adults with skeletal muscle spasm secondary to acute trauma:**

"All patients of this group received some degree of relief from the drug, and it is interesting that there was a significant degree of reduction in skeletal muscle spasm in 96% of these patients."[1]

2 **In 39 patients with herniated lumbar and cervical discs, who received methocarbamol for relief of pain and muscle spasm:**

"The response was judged to be pronounced in 25" ... "moderate" in 13. "In most instances the attacks subsided quickly, so that the patients could continue to work or go back to work sooner than expected."[2]

3 **In 17 patients with acute muscle spasm:**

"An excellent result, after methocarbamol administration, was obtained in all patients with acute skeletal muscle spasm."[3]

4 **In 30 patients with pyramidal tract and acute myalgic disorders:**

"Use of this drug (Robaxin) resulted in significant improvement in 27 (90%), questionable improvement in 2, and none in 1 . . . No side-effects developed after 72 hours on the medication."[4]

5 **In 60 industrial workers with uncomplicated skeletal muscle spasm:**

"Results were gratifying in that 55 workers, or 92%, could return to full or light duty. No side effects were encountered."[5]

Supply: ROBAXIN Tablets, 0.5 Gm., in bottles of 50.

References: 1. Carpenter, E. B.: Southern M.J. 51:627, 1958. 2. Forsyth, H. F.: J.A.M.A. 167:163, 1958. 3. O'Doherty, D. S., and Shields, C. D.: J.A.M.A. 167:160, 1958. 4. Park, H. W.: J.A.M.A. 167:168, 1958. 5. Plumb, C. S.: Journal-Lancet 78:531, 1958.

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Ethical Pharmaceuticals of Merit since 1878

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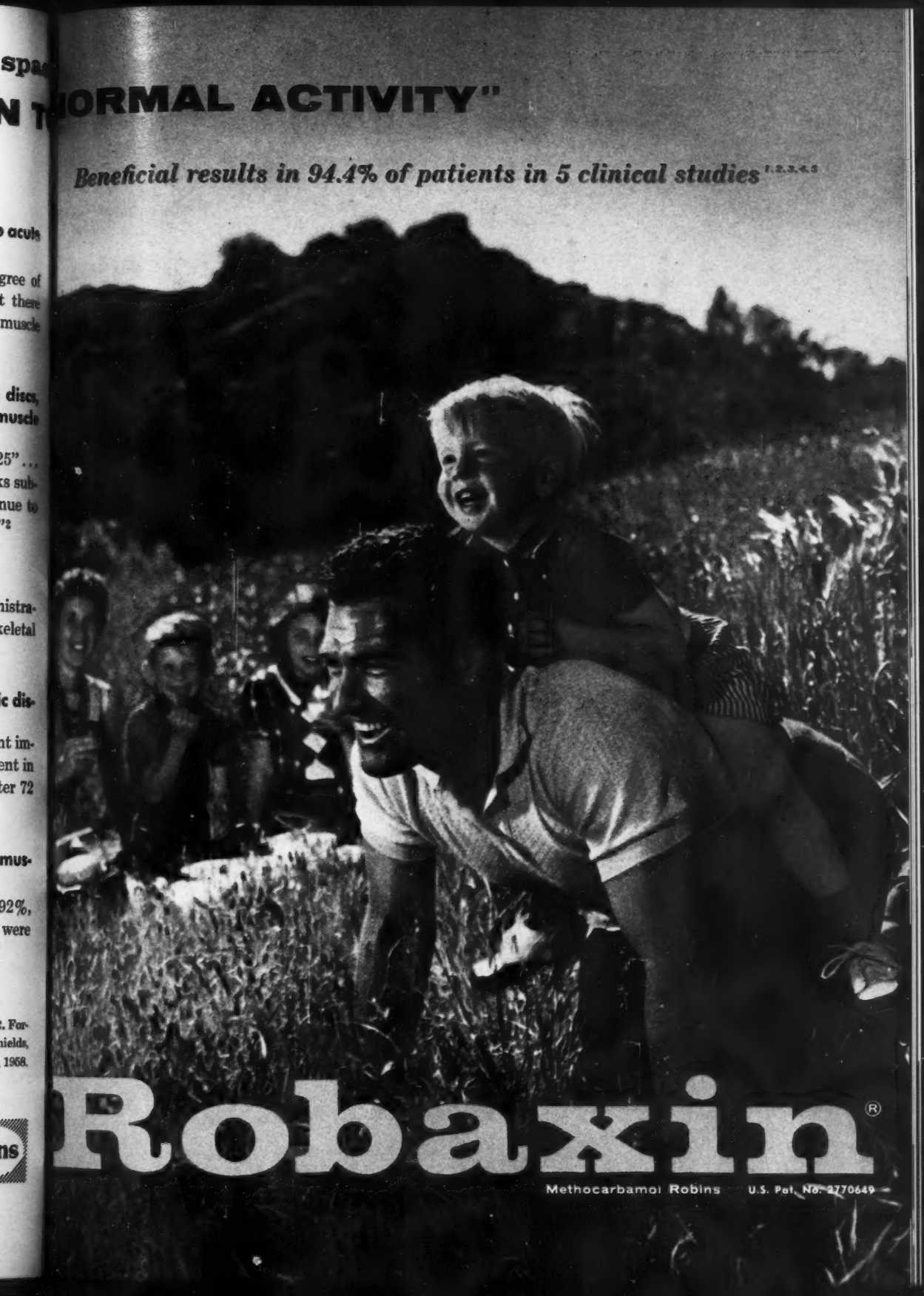
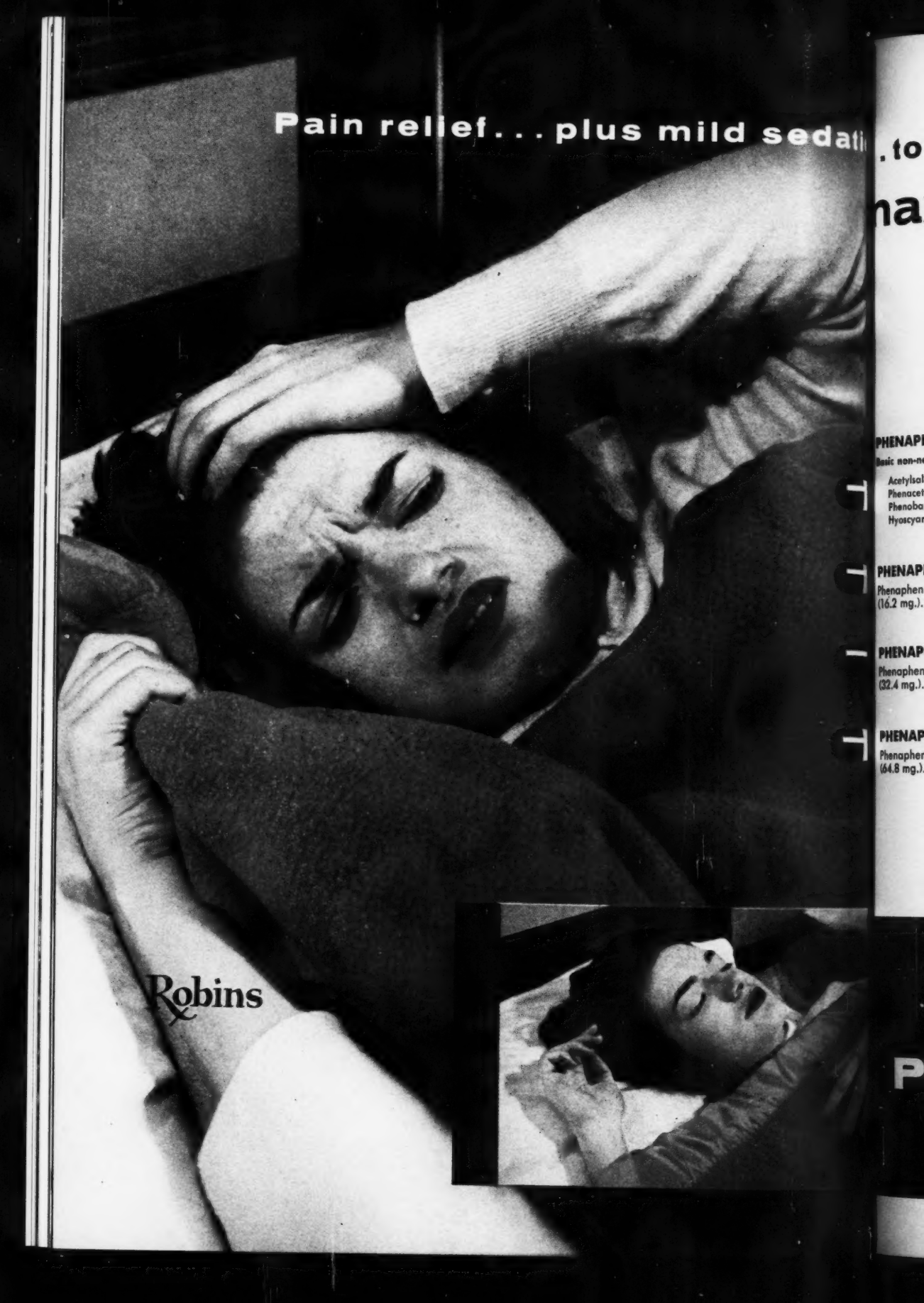

ORMAL ACTIVITY"
Beneficial results in 94.4% of patients in 5 clinical studies[1,2,3,4,5]
Robaxin®
Methocarbamol Robins
U.S. Pat. No. 2770649


Pain relief . . . plus mild sedati
Robins

. to assure
naximum safe analgesia

Pain relief—tailored to patient need—even (in many cases) eliminating the need for morphine, "the drug of last resort,"[2] through —

- **Four convenient PHENAPHEN potencies**
  — for individual selection, to match the intensity of pain
- **Flexibility of dosage**
  — for easy adjustment (1 or 2 capsules, as needed) to cope with variations in the level of pain

PHENAPHEN
Basic non-narcotic formula

Acetylsalicylic acid (2½ gr.)	162 mg.
Phenacetin (3 gr.)	194 mg.
Phenobarbital (¼ gr.)	16.2 mg.
Hyoscyamine sulfate .....0.031 mg.	

PHENAPHEN No. 2
Phenaphen with Codeine Phosphate ¼ gr. (16.2 mg.).

PHENAPHEN No. 3
Phenaphen with Codeine Phosphate ½ gr. (32.4 mg.).

PHENAPHEN No. 4
Phenaphen with Codeine Phosphate 1 gr. (64.8 mg.).

ADVANTAGEOUS COMBINATION

"Combinations of codeine with mild analgesic agents are commonly used to relieve pain refractory to the mild analgesic agent alone. Such combinations offer the advantage that pain relief may be afforded by doses of codeine that are ineffective when given alone."[1]

DOSAGE — One or 2 capsules as required.
SUPPLY — Bottles of 100 and 500 capsules.

1. Gross, E. G., and Keasling, H. H.: Postgrad. Med. 24:235, 1958.
2. Ritchie, W. P.: J.-Lancet 76:147, 1956.

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PHENAPHEN®
PHENAPHEN® WITH CODEINE

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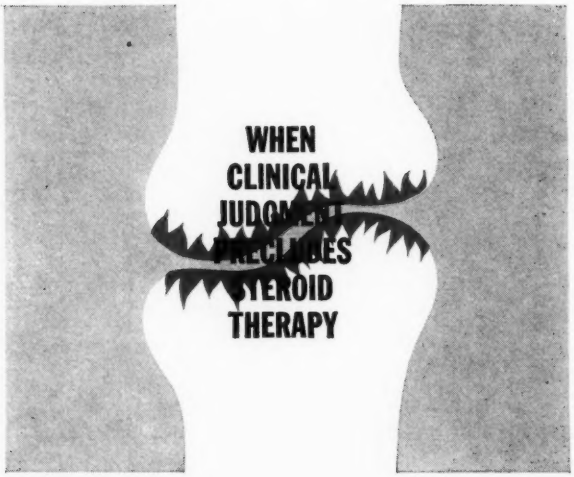

prescribe

artamide®

THE SAFE ANTI-ARTHRITIC AND ANTIRHEUMATIC THAT CONTAINS THE IMPORTANT PLUS OF ORGANIDIN® FOR THE FURTHER CONTROL OF INFLAMMATION AND TO AID IN THE RESORPTION OF NECROTIC TISSUE

Sodium-free, potassium-free ARTAMIDE is especially valuable when clinical judgment precludes steroid therapy. ARTAMIDE provides higher salicylate blood levels[1] with lower dosage. Antirheumatic, anti-inflammatory, analgesic . . . ARTAMIDE aids normal corticosteroid activity. The inclusion of ORGANIDIN, the smoother, safer, organically bound iodine, greatly increases the effectiveness of the ARTAMIDE formula by stimulating the resorptive processes[2] and further controlling inflammation. **ARTAMIDE provides symptomatic relief as well as important gains in functional capacity for many patients who cannot tolerate corticosteroids.**

Each ARTAMIDE tablet contains: Salicylamide 0.25 Gm. (4 gr.); Para-aminobenzoic Acid 0.25 Gm. (4 gr.); Ascorbic, Acid 20.0 mg. (⅓ gr.); ORGANIDIN® (iodinated glycerol) 20.0 mg. (⅓ gr.).

DOSAGE: 2 tablets 3 or 4 times daily. Requirements may vary according to the response of the patient. **SUPPLIED:** ARTAMIDE Tablets, bottles of 100 and 500. **REFERENCES:** 1. Chambers, James O.: Clinical Medicine, 61:3 (1954) pp. 203-205. 2. Salter, W. T.: A Textbook of Pharmacology, p. 603, W. B. Saunders Co. (1952).

WRITE: Professional Service Department for literature and trial supply.

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- *Prompt remission of symptoms*
- *Bleeding and frequency of stools sharply reduced*
- *Healing of rectal mucosa within a month in most cases*
- *Can be given safely over long periods of time*

Azulfidine®

BRAND OF SALICYLAZOSULFAPYRIDINE

the most valuable drug in the treatment of

Ulcerative Colitis

"The most widely accepted sulfonamide preparation today for the therapy of chronic ulcerative colitis is salicylazosulfapyridine (Azulfidine)."

Hightower, N.C., Jr., and others:
Am. J. Digest. Dis. 3:931 (Dec.) 1958

Also valuable in treatment of regional enteritis and other forms of colitis

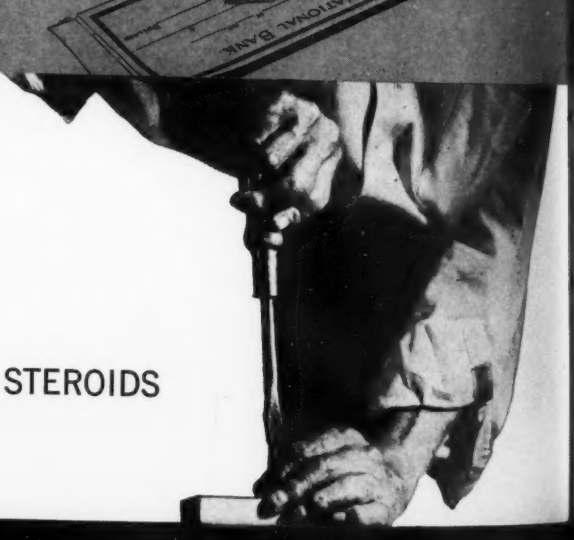
Pharmacia Laboratories, Inc.
New York City.

WITHOUT STEROIDS

In every arthritic state

WITHOUT STEROIDS

WITHOUT STEROIDS



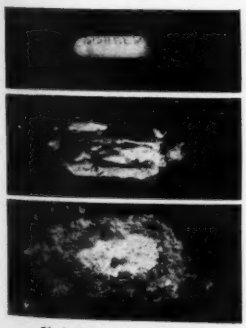
MAINTENANCE THERAPY WITHOUT STEROIDS IS FUNDAMENTAL

Sound, conservative therapy with salicylates has been consistently reaffirmed as basic, long-term maintenance therapy in the arthritides.

Buffered Pabirin provides superior maintenance therapy. It epitomizes fundamental long-term basic therapy since it can be given month after month without serious complications and with minimal problems to patient and doctor alike.

Buffered Pabirin is formulated to provide high and sustained salicylate blood levels. Each tablet consists of an outer layer containing a buffer (aluminum hydroxide), para-aminobenzoic acid, and ascorbic acid; a core of acetylsalicylic acid.

In the stomach, the outer layer quickly releases the buffer, which protects against nausea, dyspepsia and other gastrointestinal symptoms so frequently encountered with salicylates alone. The core of Buffered Pabirin then disintegrates rapidly, permitting rapid absorption of the acetylsalicylic acid for faster pain relief.



Photographs show 2-stage Tandem Release disintegration.

Each tablet contains:
Acetylsalicylic acid (5 gr.).....300 mg.
Para-aminobenzoic acid (5 gr.)....300 mg.
Ascorbic acid ..... 50 mg.
Dried aluminum hydroxide gel....100 mg.

All Buffered Pabirin is sodium- and potassium-free.

Dosage: Two or three tablets 3 or 4 times daily.

References: 1. Hart, D.; Bagnall, A. W.; Bunim, J. J., and Polley, F. H.: Ninth International Congress on Rheumatic Diseases, Toronto, Ont. (June 25) 1957. 2. Report of Joint Committee, Medical Research Council & Nuffield Foundation, Treatment of Rheumatoid Arthritis, British Medical Journal (April 13) 1957. 3. Friend, D. G.: New England J. Med. 257:278 (Aug.) 1957.

Buffered **Pabirin®** *Tablets*

SMITH-DORSEY · a division of The Wander Company · Lincoln, Nebraska · Peterborough, Canada

wherever there is inflammation, swelling, pa

VARIDASE

Streptokinase-Streptodornase Le

BUCCAL Tablet

conditions for a fast & comfortable comeback

Host reaction to injury or local infection ha
catabolic and an anabolic phase. The body respond
with inflammation, swelling and pain. In time
the process is reversed. VARIDASE speeds u
this normal process of recovery.
By activating fibrinolytic factors VARIDASE shorte
the *undesirable phase,* limits necrotic changes due t
inflammatory infiltration, and initiates the constructive phas
to speed total remission. Medication and body defense
can readily penetrate to the affected site
local tissue is prepared for faster regrowth of cells.
In infection, the fibrin wall is breached whil
the infection-limiting effect is retained. In acut
cases, response is often dramatic. In chroni
cases, VARIDASE Buccal Tablets can stimulate
a successful response to primary therap
previously considered inadequate or failing.

for routine use in injury and infection
. . . new simple buccal rout

VARIDASE Buccal Tablets should be retained in the bucca
pouch until dissolved. For maximum absorption
patient should delay swallowing saliva.
Dosage: One tablet four times daily usually for five days.
When infection is present, VARIDASE Buccal Tablet
should be given in conjunction with ACHROMYCIN® V
Tetracycline with Citric Acid.
Each VARIDASE Buccal Tablet contains: 10,000 Unit
Streptokinase and 2,500 Units Streptodornase.
Supplied: boxes of 24 and 100 tablets.

1. Innerfield, I.: Clinical report cited with permissio
2. Clinical report cited with permissio

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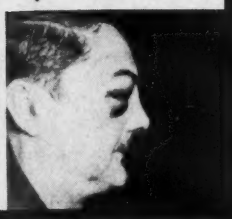
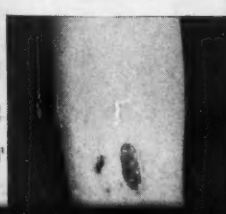


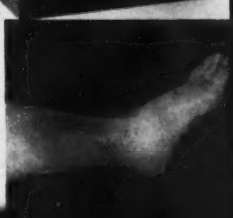
FORCE INJURY
severe bruises
...swelling
...cleared
by fifth day[2]

VARICOSE
ULCER
15 years duration
...resolved with
VARIDASE[1]

INFLAMMATORY
DERMATOSIS
rapidly spreading
rhus dermatitis
healed within
a week[1]



INFECTED
LACERATION
marked reversal
in 3 days...
returned
to school...
closure advanced[1]



THROMBOPHLEBITIS
back on his feet
in a week after
recurrent episode[1]

REFRACTORY
CELLULITIS
normal routine
resumed after 4 days
of VARIDASE[1]

in the depressed, unhappy patient

PROMPTLY IMPROVES MOOD

without excitation

- **Acts fast to relieve depression and its common symptoms:** sadness, crying, anorexia, listlessness, irritability, rumination, and insomnia.
- **Restores normal sleep**—without hang-over or depressive aftereffects. Usually eliminates need for sedative-hypnotics.

EFFICACY AND SAFETY CONFIRMED IN OVER 3,000 DOCUMENTED CASE HISTORIES.[1,2,3]

Dosage: Usual starting dose is 1 tablet q.i.d. When necessary, this dose may be gradually increased up to 3 tablets q.i.d.

Composition: Each light-pink, scored tablet contains 1 mg. 2-diethylaminoethyl benzilate hydrochloride (benactyzine HCl) and 400 mg. meprobamate.

References:
1. Alexander, L.: J.A.M.A. 166:1019, March 1, 1958.
2. Current personal communications; in the files of Wallace Laboratories.
3. Pennington, V.M.: Am. J. Psychiat. 115:250, Sept. 1958.

for depression

▲Deprol▲†

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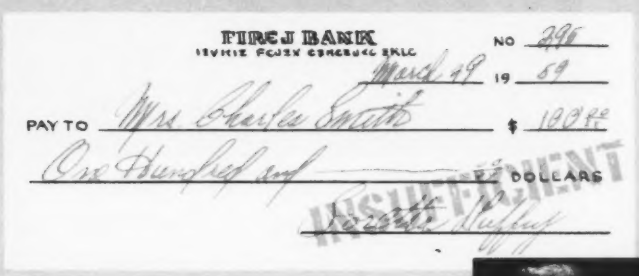
†TRADE-MARK

CD-6188

women of childbearing age... and growing children... may be

OVERDRAWN AT THE BLOOD BANK



Women of menstrual age and growing children have higher iron requirements than other individuals. Hence iron-deficiency anemias occur most often in these groups. Many clinicians recognize that most women need a hematinic for six weeks each year during reproductive years.

Livitamin, with peptonized iron and B complex, offers an excellent formula to restore depleted iron reserves in both adults and children. Peptonized iron is well absorbed and stored, and better tolerated than ferrous sulfate. B complex and other factors provide nutritional support.

LIVITAMIN®

with Peptonized Iron

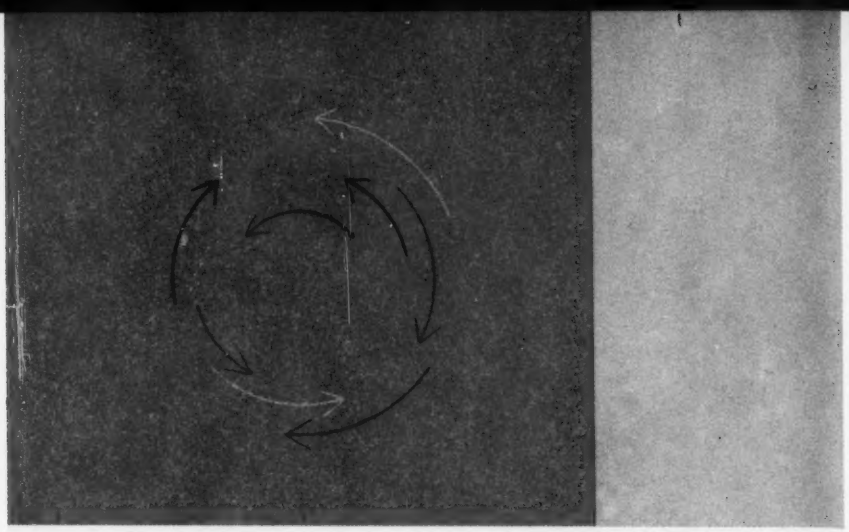
FORMULA: Each fluidounce contains:

Iron peptonized (Equiv. in elemental iron to 71 mg.)	420 mg.
Manganese citrate, soluble	158 mg.
Thiamine hydrochloride	10 mg.
Riboflavin	10 mg.
Vitamin B_{12} Activity (Derived from Cobalamin conc.)	20 mcg.
Nicotinamide	50 mg.
Pyridoxine hydrochloride	1 mg.
Pantothenic acid	5 mg.
Liver fraction 1	2 Gm.
Rice bran extract	1 Gm.
Inositol	30 mg.
Choline	60 mg.

SUPPLIED IN LIQUID OR CAPSULE.

The S.E. MASSENGILL Company

BRISTOL, TENNESSEE • NEW YORK • KANSAS CITY • SAN FRANCISCO



Livitamin assures patient acceptance because it is highly palatable. Peptonized iron provides a virtually predigested form of iron. Recent studies* show peptonized iron has these advantages:

- Rapid response in iron-deficiency anemias
- Non-astringent
- Absorbed as well as ferrous sulfate
- Better gastric toleration than ferrous sulfate
- Less constipating than ferrous sulfate

LIVITAMIN

...the preferred hematinic

*Keith, J.H.: Utilization and Toxicity of Peptonized Iron and Ferrous Sulfate, Am. J. Clin. Nutrition 1:35 (Jan.-Feb., 1957).

The S. E. MASSENGILL Company BRISTOL, TENNESSEE

NEW YORK • KANSAS CITY • SAN FRANCISO

safe . . . prompt . . . acceptable

TRIP-SUL

● viscolized at 3,000 pounds pressure to assure uniformity and stability, Trip-sul suspension is a pourable, palatable, pleasant tasting triple-sulfa of wide choice —buffered with sodium citrate to eliminate crystal formation in the kidneys.

Sulfacetamide, too!

TRIP-SUL SUSPENSION

Each fluid ounce (30 cc.) contains:

Sulfadiazine	1 gm.
Sulfamerazine	1 gm.
Sulfacetamide	1 gm.
Sodium Citrate	3 gm.

(Equivalent in buffering power of 40 grs. sodium bicarbonate)

Packaged: Pints and Gallons

TRIP-SUL TABLETS

Each pink tablet contains—

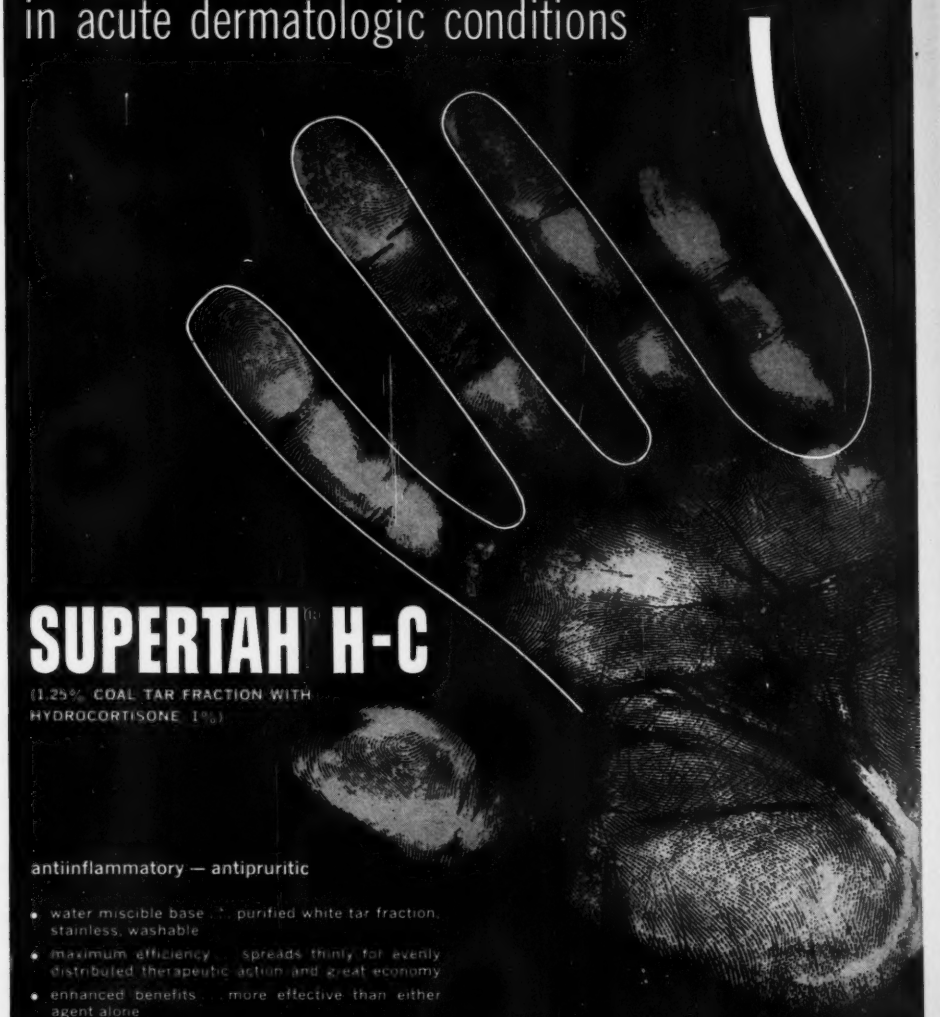
Sulfacetamide U.S.P.	166.7 mg.
Sulfadiazine U.S.P.	166.7 mg.
Sulfamerazine U.S.P.	166.7 mg.

Packaged: 100 and 1000

Carrtone Laboratories, Inc.

NEW ORLEANS, LOUISIANA

spreads
THINLY · EVENLY · ECONOMICALLY
in acute dermatologic conditions



SUPERTAH® H-C
(1.25% COAL TAR FRACTION WITH HYDROCORTISONE 1%)

antiinflammatory — antipruritic

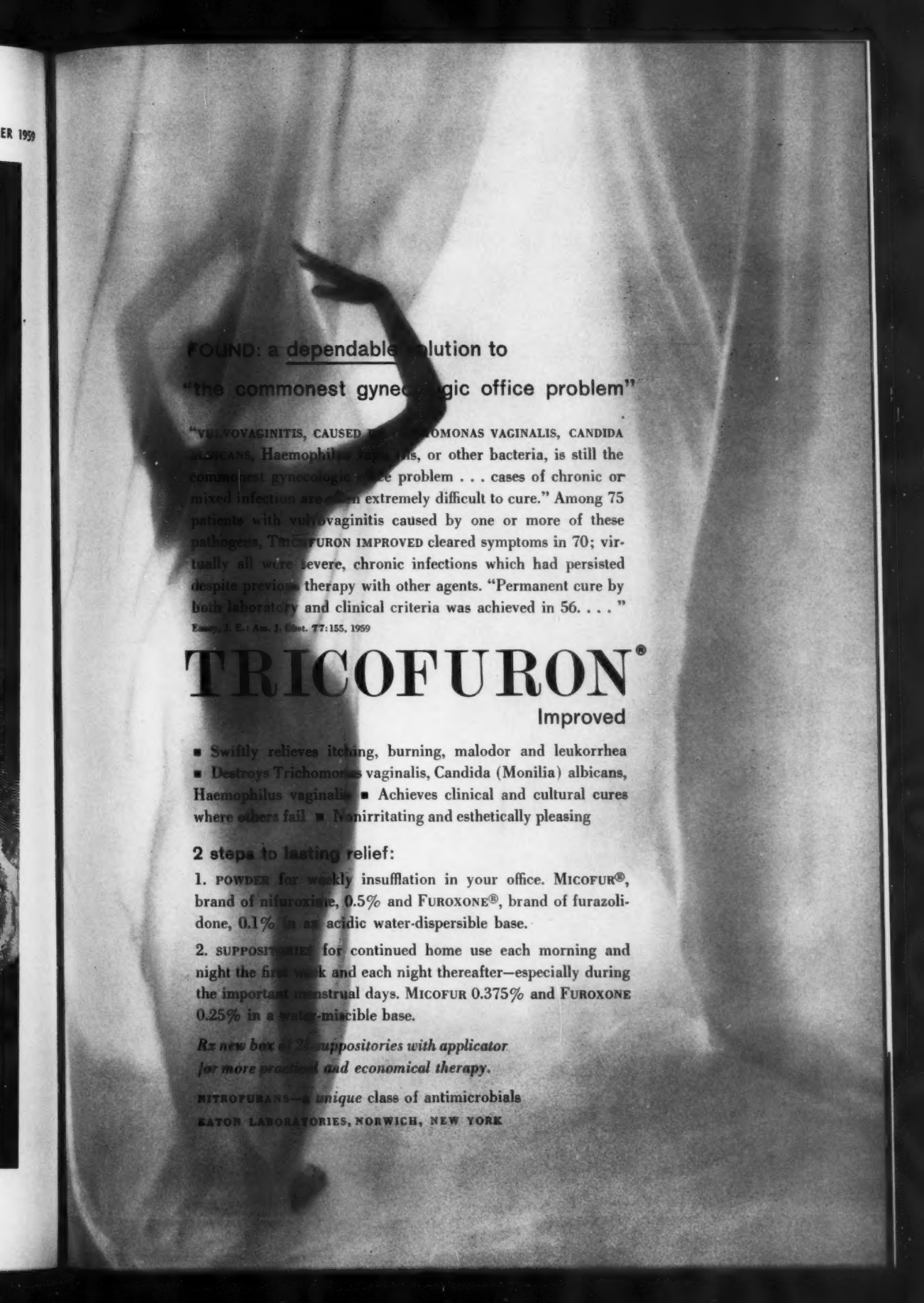
- water miscible base . . . purified white tar fraction, stainless, washable
- maximum efficiency . . . spreads thinly for evenly distributed therapeutic action and great economy
- enhanced benefits . . . more effective than either agent alone
- excellent response . . . deep penetration to source of inflammation

supplied: ½-oz. tube

also available:
SUPERTAH Ointment (1½-oz. tube)
provides the therapeutic effectiveness of time-proved tar medication
SUPERTAH S/S (with salicylic acid and sulfur; 1½-oz. tube)
for keratolytic action

All Supertah preparations are made with refined natural coal tar fraction

TAILBY-NASON COMPANY, INC. DOVER, DELAWARE


FOUND: a dependable solution to
"the commonest gynec gic office problem"
"VULVOVAGINITIS, CAUSED OMONAS VAGINALIS, CANDIDA ALBICANS, Haemophilus is, or other bacteria, is still the commonest gynecologic office problem . . . cases of chronic or mixed infection are often extremely difficult to cure." Among 75 patients with vulvovaginitis caused by one or more of these pathogens, TRICOFURON IMPROVED cleared symptoms in 70; virtually all were severe, chronic infections which had persisted despite previous therapy with other agents. "Permanent cure by both laboratory and clinical criteria was achieved in 56. . . . "
TRICOFURON®
Improved
■ Swiftly relieves itching, burning, malodor and leukorrhea ■ Destroys Trichomonas vaginalis, Candida (Monilia) albicans, Haemophilus vaginalis ■ Achieves clinical and cultural cures where others fail ■ Nonirritating and esthetically pleasing
2 steps to lasting relief:
1. POWDER for weekly insufflation in your office. MICOFUR®, brand of nifuroxime, 0.5% and FUROXONE®, brand of furazolidone, 0.1% in an acidic water-dispersible base.
2. SUPPOSITORIES for continued home use each morning and night the first week and each night thereafter—especially during the important menstrual days. MICOFUR 0.375% and FUROXONE 0.25% in a water-miscible base.
Rx new box of 24 suppositories with applicator
for more practical and economical therapy.
NITROFURANS—a unique class of antimicrobials
EATON LABORATORIES, NORWICH, NEW YORK

NIAMID*

the mood brightener

Lifts the burden of depression... opens the way for a sunnier outlook

New areas of therapy

NIAMID is clinically effective in a broad range of depressive states, including: involutional melancholia, senile depression, postpartum depression, reactive depression, the depressive stage of manic-depressive disease, and schizophrenic depressive reaction.

A wide variety of psychoneurotic depressions seen in general practice also respond effectively to NIAMID. Depression associated with the menopause and with postoperative states, and depressions accompanying chronic or incurable diseases such as gastrointestinal and cardiovascular disorders, arthritis, and inoperable cancer, can now be treated successfully with NIAMID.

NIAMID is also strikingly effective for many complaints, mild or severe, vague or well defined, which are due to masked depression rather than to organic disease. This masked depression may take the form of guilt feelings, crying spells or sadness, difficulty in concentration, loss of energy or drive, insomnia, emotional fatigue, feelings of hopelessness or helplessness, loss of interest in normal activity, listlessness, apprehension or agitation, and loss of appetite and weight.

While tranquilizers have had some measure of effectiveness in many of these areas, NIAMID now gives the practicing physician a new, safe drug for the specific treatment of depression without the risk of increasing the depressive symptoms.

New safety

NIAMID, in extensive clinical trials, has not been associated with the hepatotoxic reactions observed with the first of the monoamine oxidase inhibitors. These reactions have not been seen with NIAMID.

Acute and chronic toxicity studies show this drug's distinctive freedom from toxicity. Moreover, during the extensive clinical trials of NIAMID by a large number of investigators, not only has no liver damage been reported, but only in a very few isolated instances have hypotensive effects been seen.

The absence of toxicity may be the result of the unique carboxamide group in the NIAMID molecule. This structure may explain why NIAMID is excreted largely unchanged in the urine, with only insignificant quantities of potentially free hydrazine being formed. Previously, where a monoamine oxidase inhibitor had been associated with hepatic toxicity, there was some evidence that substantial quantities of free hydrazine were formed in the body.

Background of NIAMID

A major advance in the treatment of mental depression came with a newer understanding of the influence of brain serotonin and norepinephrine on the mood. Levels of both these neuro-hormones are decreased in animals under experimental conditions analogous to depression; relief of these models depressions is seen with a rise in the levels of both serotonin and norepinephrine.

A second advance came with the development of monoamine oxidase inhibitors, substances which raise the cerebral level of both serotonin and norepinephrine. The first of the amine oxidase inhibitors raised the cerebral level of serotonin, but did not appear to raise that of norepinephrine levels proportionately.

Pfizer *Science for the world's well-being™*

PFIZER LABORATORIES

Division, Chas. Pfizer & Co., Inc., Brooklyn 6, N. Y.

*TRADEMARK FOR BRAND OF NIALAMIDE

Attention at Pfizer Research was then directed to a new drug that would overcome this disadvantage. NIAMID significantly raises the cerebral level of *both* serotonin and norepinephrine under experimental conditions.

The dramatic discovery of NIAMID now makes available an extremely effective, safe antidepressant for the successful treatment of a full range of depressive states.

Precautions

Side effects are most often minor and mild manifestations of central nervous system stimulation, modifiable by reduction in dosage; these may take the form of restlessness, insomnia, headache, weakness, vertigo, dry mouth, and perspiration. Care should be taken when NIAMID is used with chlorothiazide compounds, since hypotensive effects have been noted in some patients receiving combined therapy—even though hypotension has rarely been noted with NIAMID alone. There has been no evidence of liver damage in patients on NIAMID; however, in patients who have any history of liver disease, the possibility of hepatic reactions should be kept in mind.

Dosage and Administration

Start with 75 mg. daily in single or divided doses. After a week or more, revise the daily dosage upward or downward, depending upon the response and tolerance, in steps of one or one-half 25 mg. tablet. Once satisfactory response has been attained, the dosage of NIAMID may be reduced gradually to the maintenance level.

The therapeutic action of NIAMID is gradual, not immediate. Many patients respond within a few days, others satisfactorily in 7 to 14 days. Some patients, particularly chronically depressed or regressed psychotics, may need substantially higher dosages (as much as 200 mg. daily has been used) and prolonged administration before responses are achieved.

Supply

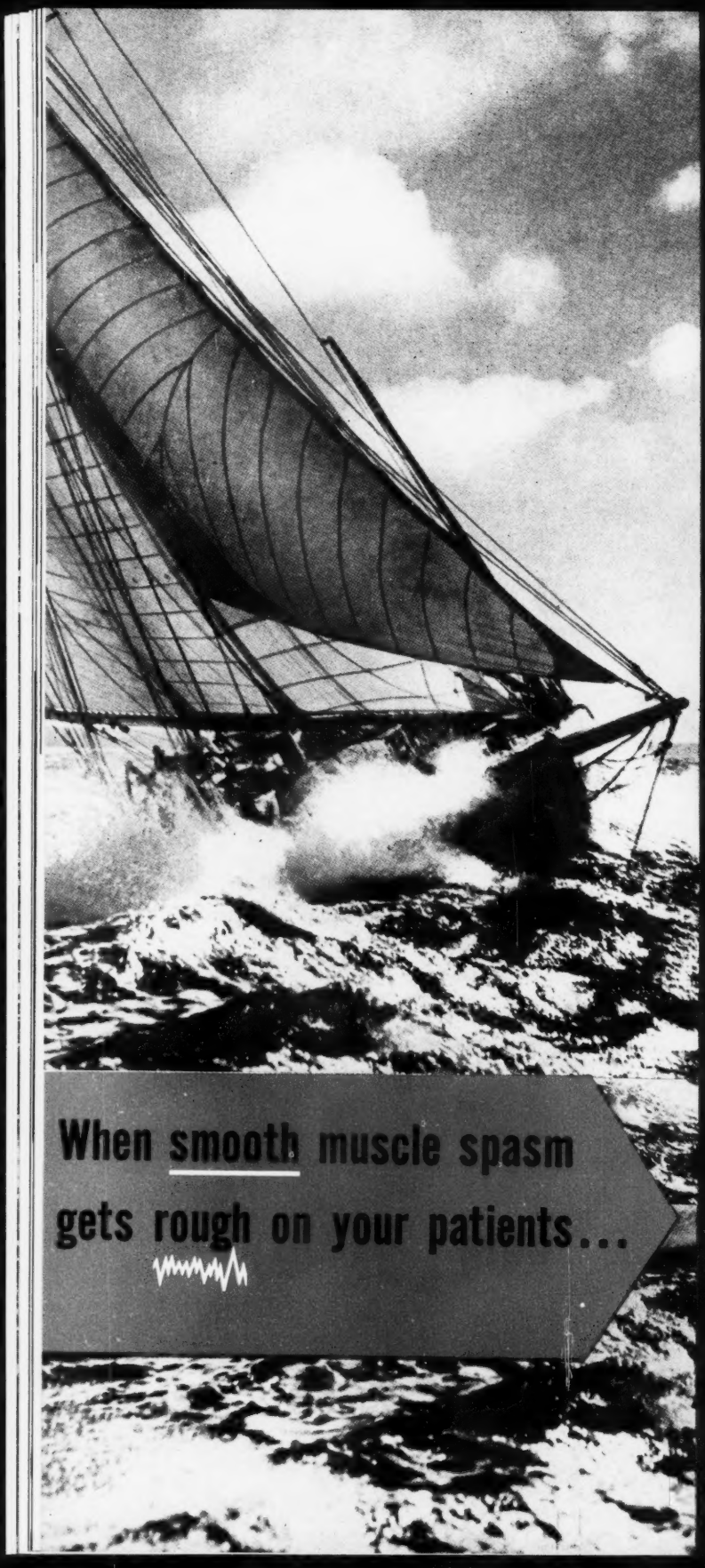
NIAMID is available in: 25 mg., pink, scored tablets in bottles of 100; and 100 mg., orange, scored tablets in bottles of 100.

References

Complete bibliography and Professional Information Booklet are available on request.

*TRADEMARK FOR BRAND OF NIALAMIDE

NIAMID
the mood brightener



Like oil on troubled waters

When smooth muscle spasm gets rough on your patients...

TABLETS • CAPSULES • ELIXIR • EXTENT

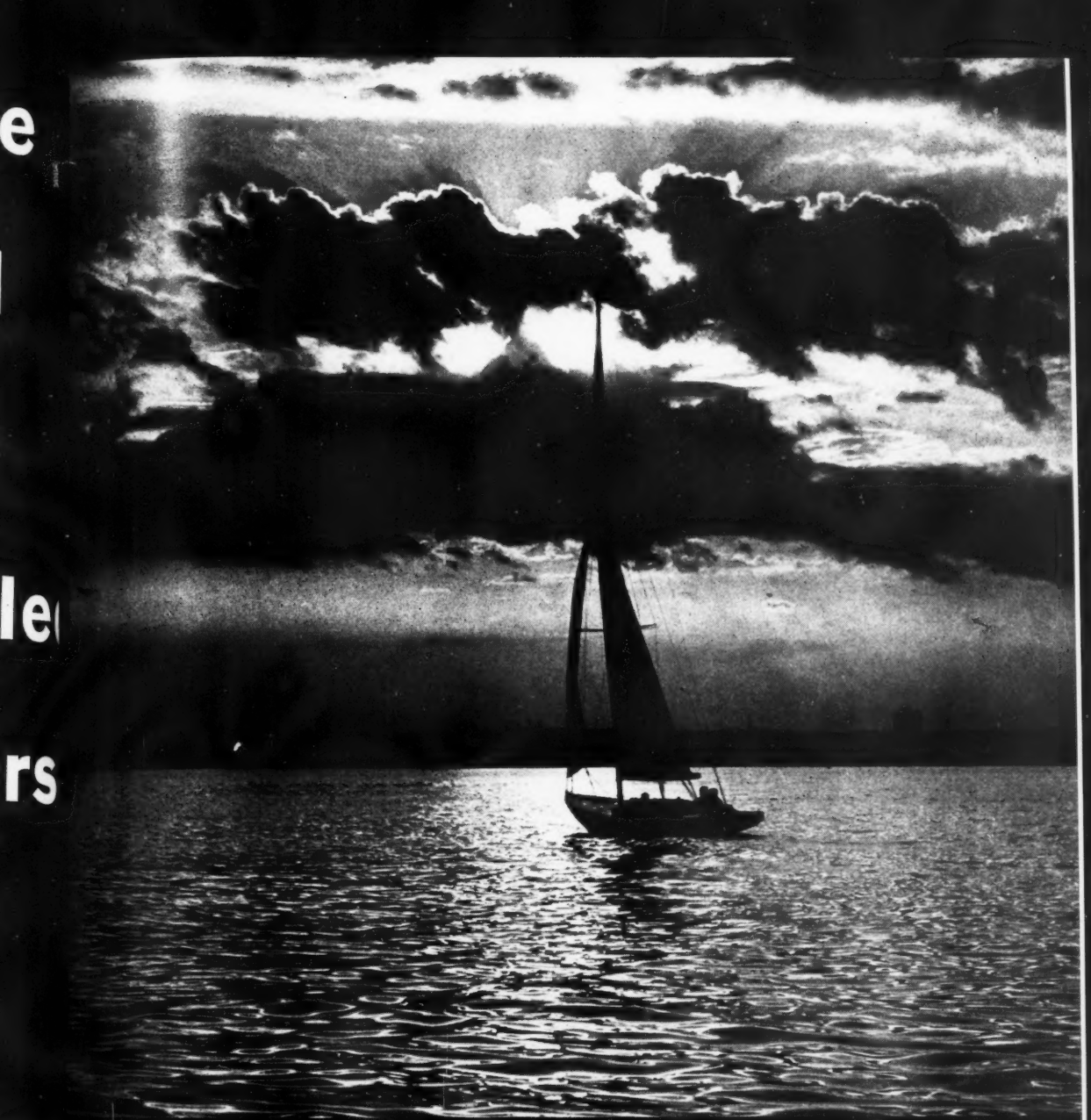
	In each Tablet, Capsule or tsp. (5 cc.) of Elixir	In Exten
Hyoscyamine sulfate	0.1037 mg.	0.3111
Atropine sulfate	0.0194 mg.	0.0582
Hyoscine hydrobromide	0.0065 mg.	0.0195
Phenobarbital	(¼ gr.) 16.2 mg.	(¾ gr.) 48.6

Prescribed by more physicia
than any other antispasmod

D

NATU

H. RO



DONNATAL®

Robins

NATURAL BELLADONNA ALKALOIDS PLUS PHENOBARBITAL

H. ROBINS CO., INC., RICHMOND 20, VIRGINIA • *Ethical Pharmaceuticals of Merit since 1878*

IT HAPPENS IN THE BEST OF FAMILIES

NOURISHED

VITERRA®

meets the specific vitamin-mineral needs of every member of the household — select the form that suits the age and condition of each patient best

VITERRA CAPSULES—comprehensive daily supplement. Bottles of 100.

VITERRA TASTITABS®—can be chewed, dissolved, or swallowed. Bottles of 100.

VITERRA THERAPEUTIC—high potency formula. Bottles of 30 and 100.

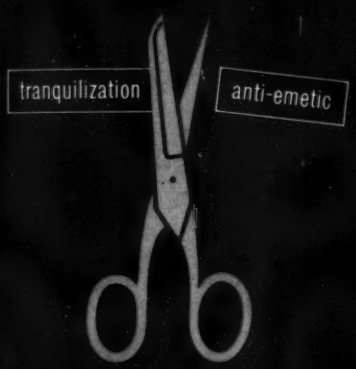
VITERRA PEDIATRIC—for infants and small children. 50 cc. Metered-Flow bottle.

Selectively formulated by one of the major producers of bulk vitamins

Rx PFRIG

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

now potent tranquilizer therapy is safer than ever



Virtual freedom of Mellaril from major toxic effects is due to greater specificity of tranquilizing action—divorced from such "diffuse" effects as anti-emetic action.

MELLARIL is virtually free of such toxic effects as

- jaundice
- Parkinsonism
- blood dyscrasia

Thiondazine [MELLARIL] is as effective as the best available phenothiazine, but with appreciably less toxic effects than those demonstrated with other phenothiazines.* This drug appears to represent a major addition to the safe and effective treatment of a wide range of psychological disturbances seen daily in the clinics or by the general practitioner.

SANDOZ

Mellaril®

THIORIDAZINE (SANDOZ)

specific, effective tranquilizer • safer at all dosage levels

remarkable lack of side effects

In more than 3,000 carefully-followed patients, Mellaril has been almost completely free of such major side effects as jaundice, extrapyramidal symptoms, Parkinsonism, blood dyscrasia, dermatitis **even when given in quantities far in excess of the usual dosage.**

"POVERTY" OF SIDE EFFECTS

"The most striking aspect of thioridazine [Mellaril] therapy is the poverty of side effects.... In its lack of side effects and low toxicity, it is superior to all other tranquilizing drugs tested. For this reason also it is well tolerated by patients, particularly those who are not hospitalized and who frequently discontinue their medication because of dizziness, sleepiness, increased tension or parkinsonism with other drugs."[2]

NEGLIGIBLE SIDE EFFECTS

"Side effects were negligible at all dosage levels: no incidence of parkinsonism or other extrapyramidal symptoms. Minimal sedation, on the whole lower than with other tranquilizing agents. No alteration in liver function, urine or blood. No photosensitivity. Patient acceptability was exceptional: lack of drowsiness, lethargy or 'washed out' feeling, permitted patients to carry on normal everyday activities. Orthostatic hypotension was absent. The initial 'keyed up' tense feeling common to other drugs of this type was absent.... Patients forced to interrupt treatment with other phenothiazine derivatives because of parkinsonism or other extrapyramidal symptoms were able to continue therapy with thioridazine without appearance of parkinsonism."[3]

SINGULARLY FREE OF SIDE EFFECTS

"The extrapyramidal syndrome was not encountered in any of its forms. Dizziness and sleepiness responded to a reduction in dosage. Other side effects did not occur.... It is singularly free from the side effects ordinarily seen with these [phenothiazine] compounds."[4]

ABSENCE OF SIGNIFICANT SIDE EFFECTS

"None of the following toxic effects, so common after administration of the phenothiazines, was present during the period of Thioridazine administration: Parkinsonism or Parkinson-like symptoms, photosensitivity, orthostatic hypotension, bone-marrow depression."[1]

MINIMAL SIDE EFFECTS

"Side effects such as extrapyramidal activity, jaundice and photosensitivity have not been observed in patients treated with Thioridazine [Mellaril]. Extrapyramidal side effects produced by other phenothiazines have disappeared promptly with no deterioration in the behavioral response when these patients have been shifted to Thioridazine."[5]

NO JAUNDICE

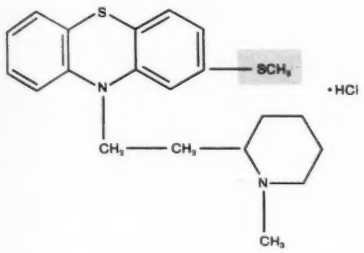
"No allergic reactions were observed such as skin eruptions, jaundice or agranulocytosis. Central nervous system toxicity, as manifested by extrapyramidal effects, seizures, and excitement did not occur despite the use of high doses (up to 2000 mg.) of the drug."[6]

Mellaril®

THIORIDAZINE

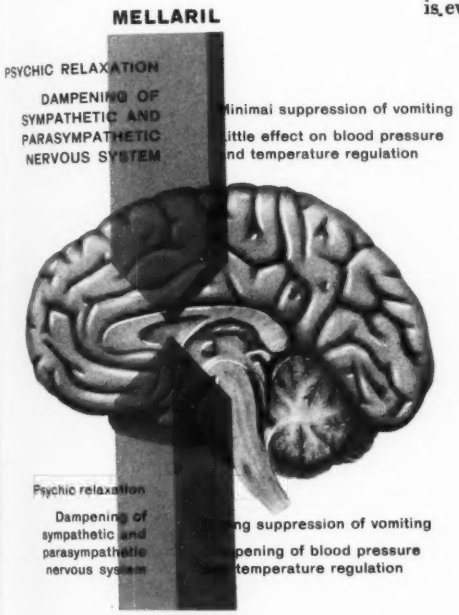
specific, effective tranquilizer • safer at all dosage levels

a new advance in tranquilization:
greater specificity of tranquilizing action plus fewer side effects

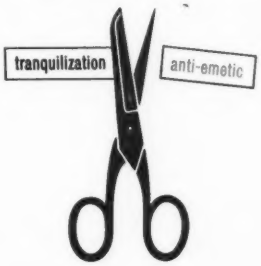


Of 109 phenothiazines synthesized by Sandoz, Mellaril was selected as the most promising on the basis of extensive evaluation. The presence of a thiomethyl radical ($S\text{-}CH_3$) in the position conventionally occupied by a halogen in other phenothiazines is unique and could be responsible for the relative absence of side effects and greater specificity of psychotherapeutic action. This is shown clinically by:

1 A specificity of action on certain brain sites in contrast to the more generalized or "diffuse" action of other phenothiazines. This is evidenced by a lack of appreciable anti-emetic effect.



other phenothiazine-type tranquilizers



2 Less "spill-over" action to other brain areas – hence, absence of undue sedation, drowsiness or autonomic nervous system disturbances.

3 A notable absence of extrapyramidal stimulation.

4 Lack of impairment of patient's normal drive and energy, while achieving psychomotor control in mental and emotional disorders.

5 Virtual freedom from toxic effects – jaundice, photosensitivity, skin eruptions, disturbed body temperature regulation, blood forming disorders have been absent in reports currently available.

These properties add up to a greater margin of safety in general office practice, in ambulatory psychiatric out-patient clinics, and in hospitalized patients.

Mellaril®

THIORIDAZINE SILO

specific effective tranquilizer • safer at all dosage levels

excellent clinical response

In office practice and in hospitalized patients, Mellaril has proved highly useful for a wide variety of major and minor emotional disorders (such as anxiety, tension, apprehension, alcoholism, agitated psychoneurosis, agitated psychotic states, etc.).

EXTREMELY SATISFACTORY "... produced extremely satisfactory results in the broad therapeutic range represented in this series."[3]

POTENT AGENT "... appears to be a potent agent in the symptomatic management of a variety of psychiatric states."[4]

MAJOR ADDITION TO THERAPEUTICS "This drug appears to represent a major addition to the safe and effective treatment of a wide range of psychological disturbances seen daily in the clinics or by the general practitioner."[1]

AN ACTIVE AGENT "Thioridazine is an active therapeutic agent.... It is effective in a variety of psychiatric disorders, including schizophrenic reactions.... The drug is particularly advantageous for a group of schizophrenic patients who are sometimes made worse by other phenothiazine derivatives or Rauwolfia alkaloids. It should also be suitable for treating patients with psychoneuroses and chronic brain syndrome."[6]

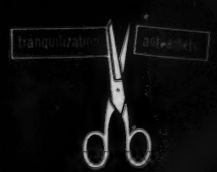
EVEN IN VERY SEVERE CASES "Of the 152 patients treated 25 have been released and they have not suffered a relapse. This proportion is significant if we stop to consider that we are dealing only with acute cases which had been considered hopeless and obviously destined to finish their days in an asylum."[7]

EXCELLENT THERAPEUTIC RESPONSE "Patients with emotional tensions resulting from the stress and strain of life ... were treated with Mellaril at the dosage level of 10 mg. three times daily. In 94 such patients, 83 obtained an excellent therapeutic response."[8]

Mellaril®

THIORIDAZINE HCl

specific effective tranquilizer • safe at all dosage levels



"...extremely satisfactory results..." in a clinical spectrum ranging from minor nervous disorders to severe psychotic disturbances[3]

RESULTS WITH MELLARIL IN 194 PATIENTS[3]

ACUTE PSYCHOTICS	CHRONIC PSYCHOTICS	NEUROTICS
83% satisfactory effect	68% satisfactory effect	57% satisfactory effect
Some cases had complete remission of symptoms. Most were able to return home to useful occupations.	Relief of symptoms in cases permitted easier management and a return to a more or less useful life.	Some cases, complete relief of symptoms. Other cases, partial relief of symptoms.

RESULTS WITH MELLARIL IN PATIENTS PREVIOUSLY TREATED WITH OTHER TRANQUILIZERS[3]

DIAGNOSTIC CATEGORY	IMPROVED %	VERY SATISFACTORY %	SATISFACTORY %	UNSATISFACTORY %
SCHIZOPHRENIA				
Acute	89	61	28	11
Chronic paranoid	84.2	31.6	52.6	15.8
Chronic, other	73.9	21.7	52.2	26.1
Residual	57.1	9.5	47.6	42.9
CHRONIC BRAIN SYNDROME	66.6	33.3	33.3	33.3
CHRONIC PSYCHONEUROSIS	62.5	12.5	50	37.5
CHRONIC PSYCHOSOMATIC DISORDERS	75	25	50	25

Mellaril®

THIORIDAZINE HCl

specific, effective tranquilizer • safer at all dosage levels

a guide to administration and dosage

Dosage ranges from 10 mg. three or four times a day in milder situations to 25 mg. three or four times a day for more disturbed patients. In ambulatory psychiatric out-patients, dosages of 50 to 100 mg. three or four times a day have been found adequate. For severely disturbed hospitalized psychotics, dosages of 200 to 300 mg. three times a day may be administered.

Dosage must be individualized according to the condition and degree of response. In all cases, the smallest effective dosage should be determined for each patient.

INDICATION	USUAL STARTING DOSE	TOTAL DAILY DOSAGE RANGE
ADULTS		
Mental and Emotional Disturbances:		
MILD—where anxiety, apprehension and tension are present	10 mg. t.i.d.	20-60 mg.
MODERATE—where agitation exists in psychoneurosis, alcoholism, intractable pain, senility, etc.	25 mg. t.i.d.	50-200 mg.
SEVERE—in agitated psychotic states as schizophrenia, manic depressive, toxic psychoses, etc.:		
Ambulatory	100 mg. t.i.d.	200-400 mg.
Hospitalized	100 mg. t.i.d.	200-800 mg.
CHILDREN		
BEHAVIOR PROBLEMS IN CHILDREN	10 mg. t.i.d.	20-40 mg.

PRECAUTIONS: Although possessing a unique structure and a selectivity of action which broadens its therapeutic ratio, the physician should be alert to the possibility of untoward reactions in certain susceptible individuals. In particular, he should watch for potential hemopoiet depression, jaundice or orthostatic hypotension. As wi other phenothiazines, Mellaril is contraindicated i severely depressed or comatose states from any cause.

SUPPLIED: MELLARIL Tablets, 10 mg., 25 mg., 100 mg. Bottles of 100.

1. Ostfeld, A. M.: Scientific Exhibit, American Academy of General Practice, San Francisco, April 6-9, 1959. 2. Kinross-Wright, V. J.: Lecture, Clini Meeting, American Medical Association, Minneapolis, Dec. 4, 1958. 3. Kinross-Wright, V. J.: Scientific Exhibit, Clinical Meeting, American Medical Asso ation, Minneapolis, Dec. 2-5, 1958. 4. Cohen, S.: TP-21, a new phenothiazine, Am. J. Psychiat. *115*:358, Oct. 1958. 5. Glueck, B.: Scientific Exhibit, Americ Psychiatric Association, Philadelphia, April 27-May 1, 1959. 6. Hollister, L. E., and Macdonald, B. F.: Presented at California Medical Association; Section Psychiatry, San Francisco, Feb. 25, 1959. 7. Remy, M.: Schweiz. med. Wchnschr. *88*:1221, Nov. 29, 1958. 8. Freed, S. C., in discussion on Thioridazine (Mellari in Psychiatric Patients, Hollister, L. E., and Macdonald, B. F., presented at California Medical Association; Section on Psychiatry, San Francisco, Feb. 25, 195

- controls neurotic and psychotic patients with anxiety, apprehension, nervous tension
- virtual absence of jaundice, parkinsonism, photosensitivity, dermatitis
- minimal sedation and drowsiness
- does not mask organic conditions such as brain tumors, intestinal obstruction, etc., because of lack of anti-emetic action
- increased specificity of action results in greater safety at all dosage levels

SANDO

Mellaril®

THIORIDAZINE HCl

specific, effective tranquilizer • safer at all dosage levels

STOP

running noses

and open stuffed noses orally

Triaminic®

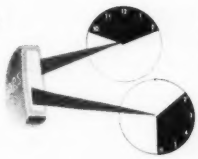
the leading oral nasal decongestant

- in nasal and paranasal congestion
- in sinusitis
- in postnasal drip
- in allergic reactions of the upper respiratory tract

safer and more effective than topical medication[1,2,3]

- systemic transport to all respiratory membranes
- provides longer-lasting relief
- presents no problem of rebound congestion
- avoids "nose drop addiction"

Relief with Triaminic is prompt and prolonged because of this special timed-release action . . . beneficial effect starts in minutes, lasts for hours



first — the outer layer dissolves within minutes to produce 3 to 4 hours of relief

then — the core disintegrates to give 3 to 4 *more* hours of relief

Each TRIAMINIC Tablet provides:
Phenylpropanolamine HCl .....50 mg.
Pheniramine maleate .....25 mg.
Pyrilamine maleate .....25 mg.

One-half of this formula is in the outer layer, the other half is in the core.

Dosage: One tablet in the morning, mid-afternoon and at bedtime.

References: 1. Lhotka, F. M.: Illinois M. J. 112: 259 (Dec.) 1957. 2. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 3. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958.

TRIAMINIC JUVELETS: Each timed-release Juvelet is equivalent in formula and dosage to one-half of a TRIAMINIC tablet, for the adult or child who requires only half strength dosage.

TRIAMINIC SYRUP is recommended for adults and children who prefer liquid medication. Each 5 ml. tsp. is equivalent to ¼ of a Triaminic Tablet. *Adults:* 2 tsp. 3-4 times a day; *children 6-12:* 1 tsp. 3-4 times a day; *children under 6:* in proportion.

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Gastrografin: In Gastroenterologic Diagnosis*

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The authors give their experiences with a new contrast medium for use in visualization of the gastrointestinal tract.

Introduction

BARIUM SULFATE, as used in diagnostic roentgenography, has certain undesirable features. These are: (1) a tendency to become inspissated and impacted in the colon with resultant discomfort to the patient and occasional serious consequences; (2) density which obscures the mucosal pattern in the filled viscus; (3) formation of inflammatory reactions and granulomas when extruded into body cavities; and, (4) difficult or impossible removal from obstructed bowel prior to operation.

Gastrografin** (diacetylamino-triiodobenzoic acid) is a recently developed radiopaque material which is free of some of these objectionable qualities. This is a report of our experience and evaluation of the usefulness, advantages and disadvantages of this medium in 100 patients to whom it was administered for diagnostic purposes.

Pharmacology and Properties of Gastrografin

Gastrografin is a lemon-flavored, 76% aqueous solution of the salt of diacetylaminotriiodobenzoic acid, with small amounts of a wetting agent (polysorbate 80 U.S.P.) and an antifoaming agent added. Studies with Gastrografin conducted at the Squibb Institute for Medical Research have shown it to have low toxicity, complete solubility in water, complete miscibility with body fluids and a lower viscosity than barium sulfate.[1]

Minimal amounts of the material are absorbed from the intestinal tract during routine radiologic examination, although visuali-

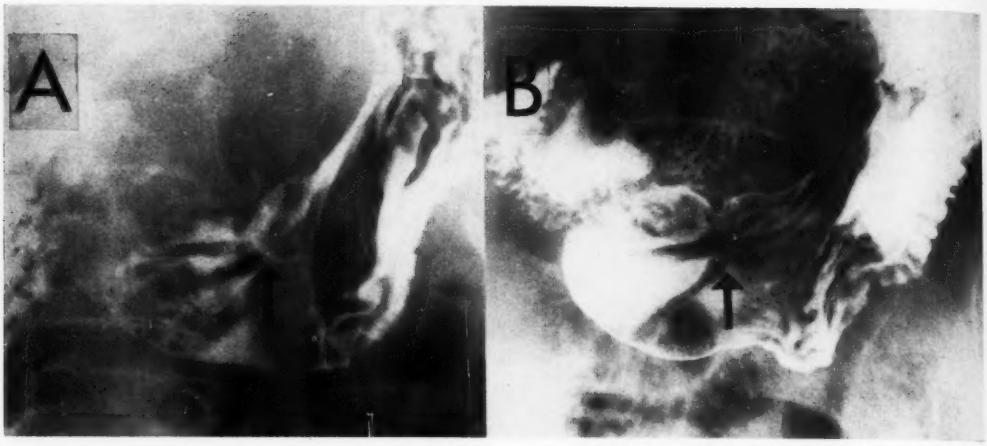
FIG. 1

(A) Carcinoma of esophagus with barium; (B) Same with Gastrografin; (C) Stricture of esophagus with barium; (D) Same with Gastrografin,—note the essentially comparable contrast.

*Read before the Section on Gastroenterology, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

**Gastrografin-Sodium and Methylglucamine Diatriozoates, E. R. Squibb & Sons.

FIG. 2



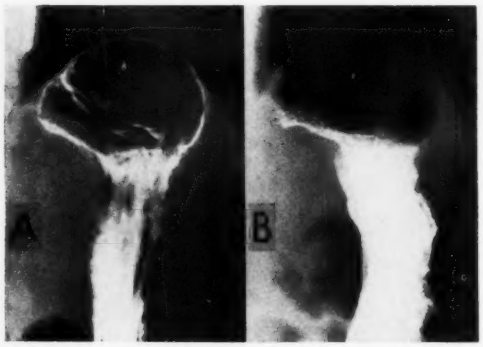
(A) Gastric ulcer shown with Gastrografin. Note satisfactory mucosal relief. (B) The same 3 weeks later with barium.

zation of the genitourinary system, following oral administration, has been reported.[2,3] We noted a falsely high protein-bound iodine the day following the administration of Gastrografin and this has also been noted previously.[3,4] It has been used for cerebral angiography, angiocardiography, translumbar aortography and intravenous urography.[5-10] Lack of toxic effects, following accidental aspiration of Gastrografin into the tracheobronchial tree, has been noted and we have confirmed this.[11,12] Post[13] reported no residual medium in the bowel or peritoneal cavity 24 hours following the extrusion of one ounce of Gastrografin through an ileal perforation.

Clinical Experience with Gastrografin

In the majority of instances Gastrografin was given by mouth, but we have also administered it as an enema in a 50% solution and by direct intubation of the duodenum, jejunum, and ileum. Initially, it was given orally in the amount of 2 ounces undiluted, or diluted with an equal amount of water. Experience showed that 4 ounces of Gastrografin undiluted gave a more satisfactory visualization for oral use. Our observations with Gastrografin are in general agreement with those reported by others.[2-4,14] We shall attempt to define these observations by descriptions of the use of this material in the various segments of the gastrointestinal tract.

FIG. 3



(A) Mucosal relief of fundus shown by barium; (B) Same with Gastrografin,—note lack of adhesiveness.

Esophagus. Gastrografin gives satisfactory visualization of the esophagus. Although transit is more rapid than with barium, this does not obviate good visualization and comparison films with barium are equal (Fig. 1).

Stomach. Gastrografin produces adequate visualization in most instances, with satisfactory mucosal relief patterns (Fig. 2). However, lack of adhesiveness of this material makes it possible to overlook small mucosal lesions (Fig. 3). The same applies to visualization of the duodenum. This material is satisfactory to show deformity and craters in most instances (Figs. 2 and 4). In comparison with barium, craters are not visualized as easily and some not seen at all fluoroscopically. It is probable that very small craters might readily be missed with Gastrografin because

of its lower viscosity and lack of adhesiveness. It is very satisfactory in patients suspected of having pyloric or duodenal obstruction. This material demonstrates retention and obstruction and is yet able to pass through high degrees of obstruction more readily than does barium, so that some knowledge of the distal bowel may also be obtained (Fig. 5).

Small Bowel. Gastrografin is not satisfactory for detailed study of the small bowel in most instances. Some lesions were observed but were better demonstrated with barium. Dilution with fluid in the gastrointestinal tract makes density such that satisfactory visualization is usually not accomplished, particularly in the distal small intestine. The maximum opacity and contrast that one sees with Gastrografin is less than with barium (Fig. 6). The small bowel is more adequately filled with Gastrografin than with barium and would probably give a better mucosal pattern if the contrast were sufficient. Gastrografin does not clump, puddle, or segment, as does barium.

FIG. 4

Duodenal ulcer shown by Gastrografin.

FIG. 5

Carcinoma of pancreas with complete clinical obstruction of duodenum. Gastrografin demonstrates obstruction and visualizes distal bowel.

Gastrografin has an unusually rapid transit through the small bowel and generally reaches the cecum in 30 to 60 minutes, often outlining the entire colon in one to three hours after oral administration. In most patients given Gastrografin in 4 ounce doses, diarrhea occurs but is not accompanied by cramping or dehydration.

Colon. In examination of the colon, Gastrografin was given by mouth and by rectum. Oral Gastrografin gives better visualization and more complete filling of the colon than does oral barium sulfate. This was helpful in a patient in whom the possibility of intestinal obstruction was suspected and the diagnosis of diverticulitis of the colon was made within 100 minutes (Fig. 7). When used as an enema, Gastrografin is not as satisfactory as barium. Its low viscosity permits a rapid retrograde flow which handicaps the fluoroscopist in detecting lesions. In a patient with carcinoma of the sigmoid, demonstrated by barium enema, the lesion was

poorly visualized by Gastrografin enema (Fig. 8).

Gastrografin is especially valuable in patients suspected of having obstruction (Fig. 9). It can be readily aspirated from the stomach or small bowel, or it may be left in the bowel without undue symptoms or complications. In a patient with postoperative obstruction of the sigmoid colon, Gastrografin remained in the colon for eight days, without causing difficulty. In suspected colonic obstruction, Gastrografin may be given by mouth without hesitation and without the necessity of a preceding barium enema.

Gastrografin is advantageous when studying patients suspected or known to have megacolon, either congenital or acquired. The great difficulty in ridding the colon of barium in patients with this disorder is well recognized. Gastrografin has been used satisfactorily in such patients and is evacuated fairly promptly without aggravating the tendency to impaction.

Discussion

In reviewing our experience in these 100 patients, it became evident that Gastrografin has definite advantages and disadvantages, compared with the use of barium, in diagnostic x-ray procedures involving the gastrointestinal tract. By far the outstanding advantage is the absence of impaction and inspissation in the intestinal tract. This factor makes it desirable for use in any case of suspected obstruction in any portion of the gastrointestinal tract. Gastrografin is indicated to obviate difficulty in ridding the bowel of radiopaque material in chronically ill and debilitated patients, elderly patients with problems of constipation, in patients about to undergo operations, and in cases of known or suspected megacolon. In suspected obstruction it circumvents the necessity of first doing an examination by barium enema. The problem may be attacked more directly and diagnosis often made more quickly, a definite advantage in a seriously and critically

FIG. 6

(A) Small bowel pattern with barium; (B) The same with Gastrografin,—note inadequate contrast and detail due to dilution of medium.

FIG. 7

Diverticulitis demonstrated with Gastrografin given orally. Possible obstruction was suspected; the correct diagnosis made in 100 minutes.

ill patient. The rapidity of transit of this material through the gastrointestinal tract affords a ready "scouting" of the entire intestinal canal so serious disease may be ruled in or out quickly in many instances. The other advantage of Gastrografin is its low order of toxicity even if accidental spillage into body cavities occurs.

While the above features indicate the desirability of using Gastrografin in many instances, there are certain disadvantages. The solubility of this material and its admixture with the fluid in the intestinal tract allows it to become so dilute in the small bowel that detailed study is not feasible. Except for suspected obstruction, it is not a satisfactory material for investigation of the small bowel. Gastrografin has a lower viscosity and a lower degree of tenacity and adhesiveness than does barium and so does not adhere to the mucosa as well. Demonstration of a small mucosal lesion, such as a duodenal ulcer, is more difficult and it is probable that some lesions will be missed. Because Gastrografin is more fluid than barium, it is entirely possible that a partial obstruction consisting of a slightly narrowed segment of bowel might be overlooked with this material but demonstrated with barium. The rapid flow, lack of adhesiveness, and dilution of this material makes it unsatisfactory as a routine use for enema study. In spite of attempts to mask the flavor of Gastrografin, most patients complain of its unpleasant taste. The majority of patients given this material by mouth developed diarrhea which in no instance presented any serious problem nor caused untoward inconvenience or discomfort to the patient. We have preferred not to administer Gastrografin to patients with marked diarrhea and have not given it to patients with ulcerative colitis. The laxative effect seems to be one of action on the small bowel rather than on the colon. The present cost of Gastrografin would also prohibit its use as a routine opaque medium.

FIG. 8

(A) Obstructing carcinoma of the sigmoid shown by barium enema; (B) The same with only questionable demonstration with Gastrografin by enema.

FIG. 9

Gastrografin demonstrating dilated ileum and space occupying mass in R.L.Q. Patient with clinical obstruction.

Summary

Our experience in the use of Gastrografin in 100 patients has been reviewed. We feel that it has a definite place in diagnostic gastroenterologic radiography. Gastrografin is indicated in any patient suspected of having a partial or complete obstruction at any point in the gastrointestinal tract, or in any patient in whom it is felt there will be difficulty in ridding the bowel of the radiopaque material. Certain disadvantages of this material are emphasized.

Acknowledgment

Appreciation is expressed to E. R. Squibb and Sons for the supply of Gastrografin used in this study.

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Pharmacodynamic Management of Cardiac Action During Deep Hypothermia*

GUNTER CORSSEN, M.D., GEORGE W. N. EGGERS, JR., M.D., JOHN R. DERRICK, M.D., and CHARLES R. ALLEN, M.D.,† *Galveston, Tex.*

In the attempt to prevent permanent damage in the central nervous system during the prolonged ischemia demanded by cardiac surgery, hypothermia has been used to depress metabolic activity. Cardiac arrhythmias present a complication of the hypothermic state. This study attempts a solution of this complication with suggestions for the management and avoidance of cardiac arrhythmias.

SINCE THE EARLY EXPERIMENTAL WORK of Bigelow and associates,[1-3] and the introduction of general hypothermia as an adjunct to anesthesia in cardiovascular and neurologic surgery by Laborit and Huguenard,[4,5] interest in the practical application of this technic has grown steadily. Numerous reports and valuable contributions on the subject have been made. The work of Swan and his coworkers[6] and the extensive data recently published by Dripps[7] appear to be most fundamental and informative.

There appears to be little doubt among the various investigators that hypothermia offers considerable protection to the central nervous system during periods of complete circulatory arrest. The most profound physiologic change in the state of low body temperature is believed to be the reduction of metabolic activity of all body tissues. The point of cooling which allows optimal metabolic reduction without residual pathologic changes in vital organs still appears to be somewhat controversial. While most authors seem to agree that temperatures below 28 to 29° C. may be harmful, recent experiments with laboratory animals reported by Kaplan and Fisher[8] and others suggest that temperatures as low as 23° C. do not necessarily cause significant damage.

Investigators agree that the most disturbing and dangerous complication during effective body cooling is the occurrence of severe cardiac arrhythmias, especially ventricular fibrillation. Since the incidence of this disturbance has been shown to be high at temperatures below 28° C., it has prevented or at least minimized the attempts at exploring clinically the possibilities of cooling to temperatures that would result in a complete cessation of all cardiac activity.

In the past, a considerable number of methods and drugs has been described and recommended for preventing or reducing the incidence of serious cardiac irregularities during deep cooling. Among the agents believed to be of definite value in decreasing myocardial irritability are the cholinergic group, such as acetylcholine and neostigmine;[9-11] the myocardial depressant drugs, such as procaine amide,[12,13] and quinidine;[14,15] as well as local anesthetic agents like procaine and lidocaine.[16,17] Also recently considered are certain barbiturates such as thiopental[18,19] and the antifibrillatory agents which are adrenolytic substances such as chlorpromazine.[11]

The importance of hyperventilation to reduce respiratory acidosis (another cause of fibrillation during the cooling procedure) has been stressed repeatedly.[6] Other measures such as sympathetic denervation of the heart and vagotomy[20] as well as vagal nerve stimulation[9] have been suggested for controlling cardiac rhythmicity during hypothermia. Perfusion of the pericardial space with warm saline solution has been thought to be of

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definite advantage for maintaining an undisturbed cardiac action during deep cooling.[8]

Numerous methods and drugs proposed for controlling myocardial irritability and eliminating the hazard of ventricular fibrillation during hypothermia seem to offer little or even no protection, whereas others appear to be of definite value in decreasing the incidence of ventricular fibrillation during cooling.

Recent work performed in our laboratory with mepazine,* a N-methyl-piperidyl-(3)-methylphenothiazine given to laboratory animals under cyclopropane-oxygen anesthesia, strongly suggests that this compound provides a specific protection of the heart against epinephrine-induced arrhythmias by reducing myocardial irritability.[22] Since it could be expected from these experiments that the drug would offer similar protection to the myocardium during deep hypothermia, this study was carried out.

Materials and Methods

Thirty-three mongrel dogs of both sexes, weighing between 5 kg. and 16 kg. (average weight 10.0 kg.) were used in this study. The animals were anesthetized with cyclopropane-oxygen mixtures and tracheal intubation was performed to insure an open airway. Immediately prior to and during the early cooling mepazine was administered intravenously in divided doses, the total dosage averaging 30 mg. per kg. in the first group of 13 dogs. In a second group (20 animals) mepazine, in a total dosage of 25 mg. per kg. diluted in 75 to 150 cc. of a 5% glucose solution, was administered in a continuous intravenous drip which was started after light surgical anesthesia was established. Eighteen dogs of this group received in addition to the mepazine, 0.2 mEq. per kg. of potassium chloride calculated to raise the plasma potassium one milliequivalent. The potassium chloride was added to the mepazine glucose mixture. The intravenous administration of the drugs was completed before reaching temperature levels below 26° C. Cooling was induced by immersing the dog in ice water. A separate ice pack was placed around the head of the animal.

The cyclopropane-oxygen mixture was administered by the to-and-fro absorption technic and maintained only during the early part of the cooling procedure. Usually at 26° C., the animal was slightly hyperventilated with 100% oxygen. Rate and force of ventilation were gradually slowed as metabolic activity of the organism decreased and discontinued as soon as the circulation was observed to be ineffective. Right-sided thoracotomy was performed at temperatures ranging from 26° to 28° C. Tapes were placed around the superior and inferior venae cava in order to regulate venous inflow and to aid in preventing distention of the heart. The azygos vein was ligated routinely.

The animals remained in ice water until body perfusion was ineffective or complete cessation of cardiac activity had developed. This occurred in most instances at temperatures ranging from 16° to 21° C. Circulatory arrest was maintained for an average duration of 45 minutes after which efforts were made to re-establish the heart action. The dog was removed from the ice bath and rewarming accomplished by perfusing the right chest and the pericardium with warm balanced salt solution. Starting with perfusion solutions at 25° C., progressively warmer solutions were used up to 40° C. In the last 16 dogs total body warming was used as the method of rewarming by replacing the ice water in the bath with warm water at temperatures gradually increasing up to 42° C. Ten dogs of this group received epinephrine (5 mg. diluted in 125 cc. of normal saline) intravenously during the rewarming phase.

Continuous temperature readings were obtained throughout the cooling procedure with a multiple lead thermometer. Thermocouples were inserted into the esophagus and in five instances additional leads were inserted into the frontal brain via the orbital fossa. In five instances the right atrial pressure was also monitored. In 27 dogs a polyethylene catheter was introduced via the femoral vein into the inferior vena cava for the withdrawal of blood samples for analysis of blood gases such as carbon dioxide, oxygen and cyclopropane, as well as for determination of pH, sodium, potassium and calcium of the plasma.

Results

A general survery of 33 animals which were subjected to deep cooling is given in table 1

*Pacatal (Warner Chilcott Laboratories, Morris Plains, N. J.)

As revealed by this table, circulatory arrest occurred at an average temperature level of 19.6° C. The lowest temperature reached before cardiac standstill developed was recorded at 14.5° C. The duration of circulatory arrest with ineffective perfusion pressure varied from 7 minutes to 92 minutes with an average duration of 45.9 minutes.

During the phase of deep cooling, usually prior to the point of progressively ineffective ventricular beats, there invariably developed certain disturbances in the formation and conduction of impulses of the heart, including auricular flutter, retrograde atrial contraction, nodal rhythm and complete heart block with idioventricular rhythm. The same development was observed during early rewarming.

Ventricular fibrillation during cooling occurred in 13 of the 33 animals (39.4%). Fifty-eight per cent of the group of 13 dogs to which mepazine alone was administered in divided doses fibrillated during the cooling phase, as compared to an incidence of 30% in the remainder of the animals to which mepazine combined with potassium chloride was given as a continuous intravenous drip. The highest temperature at which cardiac fibrillation was observed was 26.5° C., the lowest at 19.4° C. The latter occurred in conjunction with cardiotomy performed at the point of cardiac standstill.

During the rewarming procedure fibrillatory activity of the heart muscle was observed in 8 instances, 7 of which occurred in conjunction with the perfusion of hot salt solution through the chest cavity. Only one animal went into ventricular fibrillation during the rewarming phase when the total body warming technic was used. In this particular

TABLE 1

SUMMARY OF DATA OF 33 DOGS SUBJECTED TO DEEP COOLING

Dog Number	Mepazine in mg./kg. Div. Doses	Mepazine in mg./kg. In 5% Dextrose Water	KCl 0.2 mEq. Added to I.V. Drip	Lowest Esophageal Temp. (Centigrade)	Length of Ineffective Perfusion Pressure (Minutes)	Fibrillation During Cooling Temp.	Fibrillation During Warming Temp.	Sinus Rhythm Restored	Rewarming Chest Perfusion	Rewarming Total Body Warmth	24 Hours Survival
1	10	—	—	14.5	66	—	20.0	yes	+	—	—
2	15	—	—	17.0	48	21.4	—	yes	+	—	+
3	12.5	—	—	21.4	92	26.0	25.0	yes	+	—	+
4	30	—	—	15.8	82	—	—	yes	+	—	+
5	20	—	—	19.5	75	—	—	yes	+	—	—
6	30	—	—	23.6	60	26.5	—	yes	+	—	+
7	40	—	—	24.4	31	25.4	25.0	yes	+	—	—
8	30	—	—	19.0	50	—	—	yes	+	—	+
9	40	—	—	20.0	60	20.0	22.0	yes	+	—	—
10	40	—	—	19.8	17	—	—	yes	+	—	+
11	40	—	—	19.7	42	—	—	yes	+	—	+
12	40	—	—	25.0	—	25.0	—	no	+	—	—
13	30	—	+	21.0	60	21.3	21.0 to 26.0	yes	+	—	—
14	—	25	+	19.5	34	19.4	—	yes	+	—	—
15	—	27	+	18.0	31	—	—	yes	+	—	+
16	—	35	+	21.5	7	16.0	22.3	yes	+	—	—
17	—	27	+	19.9	—	—	20.0	no	+	—	—
18	—	25	+	19.0	38	—	20.0	no	—	+	—
19	—	28	+	20.3	28	—	—	yes	—	+	+
20	—	26	+	19.0	36	—	—	yes	—	+	+
21	—	30	+	19.0	56	—	—	yes	—	+	—
22	—	28	+	19.0	35	—	—	yes	—	+	—
23	—	27	+	15.9	53	—	—	yes	—	+	—
24	—	15	+	19.5	39	19.5	—	yes	—	+	+
25	—	27	+	19.5	84	—	—	yes	—	+	—
26	—	25	+	18.0	58	—	—	yes	—	+	—
27	—	27	+	20.9	—	22.1	—	no	—	+	—
28	—	28	+	17.8	58	19.8	19.0	yes	—	+	—
29	—	25	+	19.4	49	—	—	yes	—	+	+
30	5	20	+	21.0	8	—	—	yes	—	+	+
31	5	20	+	18.1	10	—	—	yes	—	+	+
32	5	20	+	20.0	25	—	—	yes	—	+	+
33	5	20	+	21.5	—	23.5		no	—	+	—

instance fibrillatory activity of the heart was only transitory and a regular sinus rhythm spontaneously developed with further warming of the animal.

No ventricular fibrillation occurred in the temperature range of 27° to 28° C.

As revealed in table 1, sinus rhythm with effective heart beat was restored in 28 of the 33 animals (84.8%).

Fifteen dogs survived the experiment (45.4%). Those animals which completely recovered from the experiment and lived 24 hours after closure of the chest were considered to have survived.

Figure 1 presents data from a typical cooling procedure (Dog No. 20), listing temperature readings, systolic and diastolic pressure values and mean arterial pressures as well as changes of the heart rate. Blood samples were drawn at different phases of the experiment marked by an arrow. As revealed by this graph the drop in blood pressure and heart rate coincides with the declining body temperature. The average cooling time from the beginning of icing to the first cardiac standstill was 72 minutes. It can be seen from figure 1 that in this particular instance 111 minutes elapsed from the time the blood pressure dropped below 40 mm. Hg. systolic to the return of the blood pressure to the same level during rewarming.

Carbon dioxide, oxygen and cyclopropane

FIG. 1

CORRELATION OF BLOOD PRESSURE, HEART RATE AND ESOPHAGEAL TEMPERATURE DURING COOLING AND REWARMING (Dog # 20)

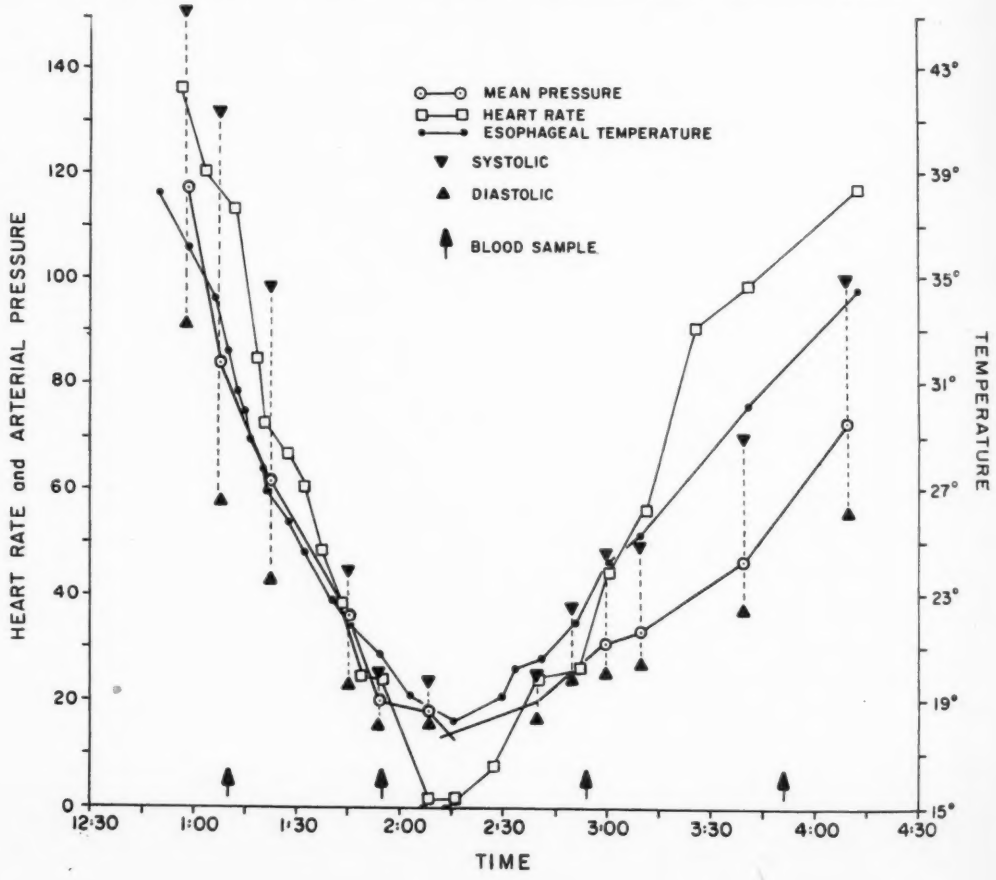
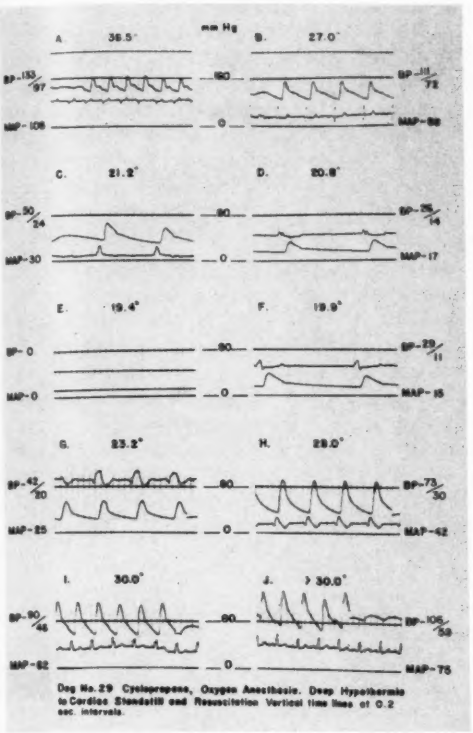


FIG. 2



contents of whole blood drawn from the inferior vena cava near the heart are listed in table 2 (Dog No. 20). As seen from this table deep cooling did not affect the hematocrit significantly. As observed by others[3,6] carbon dioxide accumulated as the circulation slowed. With rewarming and re-establishment of effective circulation the carbon dioxide was eliminated. The oxygen tension dropped from 13.9 to 3.55 vol. % at 20° C. and rose slightly during rewarming. Cyclopropane levels of the blood dropped progressively throughout the experiment being the lowest at the time of closure of the chest (1.8 vol. %).

Table 3 illustrates the changes of pH values

TABLE 2

	Temperature	*Hematocrit*	*CO_2 (mM/L)*	*Oxygen Vol. %*	*Cyclopropane Vol. %*
Early cooling	33.6°	33.5	18.8	13.9	4.7
Near standstill	20.0°	35.0	19.36	3.55	3.7
Rewarming	22.0°	29.0	14.35	5.56	3.6
Closing chest	31.4°	36.0	11.65	6.28	1.8

TABLE 3

	Temperature	*pH*	*CO_2(mM/L)*
Early cooling	33.6°	7.50	18.8
Near standstill	20.0°	7.32	19.4
Rewarming	22.0°	7.22	14.4
Closing chest	31.4°	7.28	11.7

of the blood as observed in one animal (Dog No. 20). As a rule the lowest pH level was noted during rewarming with gradual rise during the end of the experiment as shown with this animal.

During the cooling procedure no significant changes were observed in the sodium and potassium blood levels (Table 4, Dog No. 20). While the potassium content rose to its highest peak during early rewarming the sodium and calcium levels fell. The continuous addition of glucose throughout the procedure seemed to result in the later fall of plasma potassium with a simultaneous increase of sodium and calcium as has been observed earlier by others.[22] The calcium/potassium ratios did not show any significant deviation during the deep cooling phase and the rewarming phase.

Figure 2 illustrates sequences of electrocardiographic and arterial blood pressure recordings of one animal (Dog No. 29) through the various phases of cooling and rewarming (total body warming method). These phenomena were typical of all animals studied.

Discussion

The main reason for reluctance to accept the technic of hypothermia is founded in the ever-present threat of the development of serious cardiac irregularities, especially ventricular fibrillation, during deep cooling. The incidence of fibrillation during deep cooling appears to vary markedly with the anesthetic agent used.

The technic described above appears to offer a relatively simple method for reducing

TABLE 4

	Sodium mEq./L.	*Potassium mEq./L.*	*Calcium mEq./L.*	*Ca/K Ratio*	*Sugar Mg. %*
Early cooling	152	3.04	4.7	1.55	250
Near standstill	150	3.15	4.9	1.55	462
Rewarming	138	5.82	4.4	0.75	741
Closing chest	146	2.60	5.0	1.92	588

the danger of cardiac fibrillation in dogs at temperature levels below 28° C. Mepazine given as an intravenous drip during the cooling procedure appears to reduce myocardial irritability. The degree of myocardial protection, the mechanism of which is still not completely elucidated,[21] seems to be significant enough to allow cooling to temperatures at which cessation of circulation and cardiac standstill occur. Rewarming of the animal leads to a gradual re-initiation of the heartbeat and restoration of circulation.

The cardiovascular effects of hypothermia as seen in this series are essentially the same as reported by other observers.[1-6] A progressive decrease in heart rate and blood pressure with cooling and an unpredictable increase of central venous pressure were observed. The control of the latter offered a serious problem which we believe was at least partially solved by control of the venous inflow to the heart during the time of ineffective ventricular beats. It appeared to be of utmost importance to prevent any over-distention of the heart muscle during the phase of inadequate perfusion pressure. Whenever distention of the heart occurred, invariably the attempts at resuscitation were hampered.

Intravenous mepazine can cause transient falls in blood pressure[23] as was observed in the first group of 18 dogs (Table 1). However, with the administration of mepazine by slow intravenous drip no hypotension was noted.

Characteristically with cooling the electrical activity and conductivity of the heart were progressively diminished. This was evidenced by electrocardiographic changes such as prolongation of the P-R interval, prolonged QRS complex, prolonged S-T interval and T-wave changes. In deep hypothermia the P-wave disappeared and the pacemaker shifted first to the A.V. node (Fig. 2, C) and ultimately to the ventricle itself (Fig. 2, D). Ordinarily in temperature ranges from 20 to 25° C. certain areas of the heart show hyperexcitability displayed as multifocal ventricular extrasystoles and finally ventricular fibrillation. A marked reduction and even disappearance of ectopic foci of irritability was observed in a considerable number of dogs. This phenomenon was believed to be primarily due to the myocardial effect of mepazine.

Mepazine produces alterations in electrical activity of the heart similar to those produced by quinidine. There is a slowing of atrial rate, prolongation of conduction within the ventricle and decreased irritability of the myocardium.[24] These electrocardiographic effects of mepazine are most profound when large doses are used such as 40 to 60 mg. per kg. in dogs.[25] In the presence of hypothermia and with dosages used in this study the effects of mepazine appeared to be primarily the reduction of myocardial irritability.

The influence of potassium chloride in preventing excessively low pH values was evident. In all animals receiving only mepazine it was found that the pH fell with deep cooling to extremely low levels. During the early phase of rewarming, pH readings of 7.07 to 7.05 were not uncommon. This development was believed to be due to metabolic acidosis. With the addition of potassium chloride to the mepazine-glucose infusion, the pH during cardiac standstill and shortly thereafter was maintained above 7.3 with only rare exceptions.

Although it was possible to produce cardiac arrest with the absence of effective perfusion pressure for an average of more than 41 minutes in 15 animals of this series and to revive the dogs without any detectable signs of brain damage, we believe that it is neither advisable nor necessary to achieve complete cessation of the circulation for the purpose of providing a bloodless operating field for cardiovascular surgery. There was evidence that it is considerably more difficult to restore sinus rhythm following complete cardiac standstill than it is in instances in which the heart still beats occasionally. The benefits to be gained with further cooling after ineffective heart action develops do not seem to justify the greater risk encountered during this most hazardous part of the cooling procedure. We, therefore, stop cooling at the point of ineffective ventricular contraction. The aortic pressure at this phase is usually noted to be approximately 20 to 30 mm. of Hg., which will facilitate the maintenance of a relatively bloodless field during a surgical procedure.

Although this method of minimizing cardiac irregularities and especially ventricular fibrillation during deep cooling is not complete in its refinements at this time, it seems to show promise for application in cardiac and vascular surgery.

Summary

A technic for supercooling animals to the point of complete arrest of cardiac activity is described. Mepazine and potassium chloride are administered in a continuous intravenous drip while the animal is immersed in ice water.

In 33 dogs subjected to this method, cessation of circulation occurred at the average temperature level of 19.6° C. The average duration of circulatory arrest was 45.9 minutes. In order to prevent distention of the heart muscle venous inflow was controlled throughout the period of ineffective circulation. A method of total body warming was used for the restoration of normal body temperatures in the animals in the latter part of the study and found to be safer and more efficient than the method of chest perfusion with warm balanced salt solution used earlier in the series.

Fifteen dogs survived the experiment (45.4% of the total). Ventricular fibrillation was the main cause of failure to revive the animals after cardiac arrest had occurred. Effective heart action with sinus rhythm was restored in 28 of the 33 animals. Electrolyte control was important in the deep cooling phase and during early rewarming.

There was evidence that it is considerably more difficult to restore sinus rhythm following complete cardiac standstill than it is in instances in which the heart still beats occasionally. Future application of this method to facilitate cardiovascular surgery in a bloodless field will call for the avoidance of complete cardiac arrest and the maintenance of occasional ventricular contractions by the cessation of further cooling as soon as the heart fails to contract effectively.

Acknowledgment

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CASE REPORT

Tricuspid Atresia: A Case Report of a 51 Year Old Woman Treated by an Extracardiac Shunt

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A 51 YEAR OLD HOUSEWIFE was first seen in the National Children's Cardiac Hospital in March, 1953, at the age of forty-six. She had been referred to the hospital with a diagnosis of congenital heart disease.

History: Insofar as the patient knows, she was not cyanotic at birth. Cyanosis was first definitely noticed by her mother at the age of 6 years. Also at that time she was observed to become very dyspneic on the slightest effort. Clubbing of the fingers and toes had been present as far back as the patient can remember. She is a member of a rather large family—three sisters and two brothers all of whom are apparently healthy.

During her early years, from the time that cyanosis and dyspnea were first obvious, this patient's activities were severely limited because of her symptoms. However, after the age of puberty, for some unexplained reason, her tolerance to exercise increased and she was able to carry on through her teens in a fairly satisfactory fashion. She worked during much of her young adult life, married, and at age 41 was delivered of a 7 months premature baby who is living and well. This delivery was uneventful except for the administration of oxygen during delivery.

For the past few years dyspnea and cyanosis have become progressively worse. Photophobia and frequent throbbing headaches were only temporarily relieved by venosection performed in Nov. and in Dec. of 1952.

Physical Examination: This shows a well-nourished and well-developed woman in no distress at rest. She has marked cyanosis of the lips, beds of the fingernails, and toenails. The conjunctiva is congested.
Lungs: These are clear to auscultation and percussion.
Heart: The P.M.I. is in the fourth left intercostal space inside the midclavicular line. There are no thrills; regular sinus rhythm is present; the second heart sound is clear; no murmurs are heard; the pulse is 76; the blood pressure 110/80.
Abdomen: The liver and spleen are not palpable.
Extremities: There is no edema. There is marked clubbing of the fingers and toes with cyanosis.

Laboratory Examinations: The Hgb. is 23.6 Gm. and hematocrit 76 per cent. The ECG showed wide and notched T-waves (Fig. 1). The P-R interval was 0.16 seconds. There was marked left axis deviation.

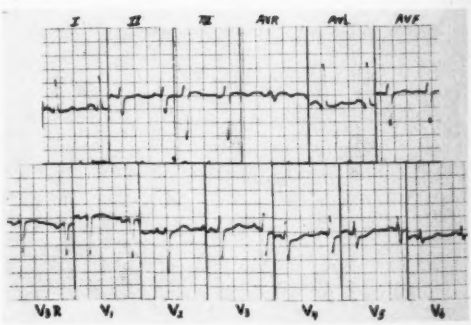
X-Ray Examination and Fluoroscopy: (Fig. 2). The lungs are clear, especially toward the periphery. There appears to be a right pulmonary artery but no pulsations are seen in its secondary branches. The heart is relatively small with no definite enlargement of any chamber except for a slight prominence of the right atrium. There is a concavity of the left upper border. In the left anterior oblique view the right ventricle appears small or absent. The pulmonary window is clear. The aortic arch is on the left.

Catherterization procedure was carried out on Feb. 10, 1953 (Table 1). The catheter was passed via the left medium basilic vein through the superior vena cava into a large right atrium. The right ventricle could not be entered but the catheter was passed repeatedly with ease from the right atrium through what appeared to be a large septal defect into the left atrium and down into the left ventricle.

Diagnosis:
Etiologic: *Congenital heart disease*
Anatomic: *Tricuspid atresia*
Physiologic: *Regular sinus rhythm*
Functional: *3D*

The patient was followed for a period of 5 years.

FIG. 1



Electrocardiogram: Note wide, notched P-waves, the P-R interval 0.16 sec., and the marked left axis deviation.

†From the National Children's Cardiac Hospital, Miami, Fla.

TABLE 1

CARDIAC CATHERTERIZATION STUDIES (February 1953)

Catheter Position	*O_2 Content Vols. %*	*% O_2 Saturation*	*mm. of Hg. Pressure*	*Mean*
Pulmonary vein	31.1	96.8	7/1	4
Left ventricle	27.7	86.3	100/6	40
*Left ventricle	27.4	85.3	105/6	40
Left atrium	27.8	86.6	8/1	4
Left atrium	26.6	82.8	5/0	2
Right atrium	23.7	73.8	7/0	3
Superior vena cava	22.1	68.8	7/2	4
*Brachial artery	27.1	84.4	105/72	

*Simultaneous samples

Her symptoms progressively worsened and in 1957, despite the fact that she had had frequent phlebotomies because of the increase in hematocrit, she developed cerebral thrombosis with paralysis of the right side of the face and loss of speech. She recovered from this without residua. Her symptoms of headache, photophobia, and dizziness progressed.

During this period surgery had been considered but rejected because of the patient's age and the presumed high risk that such a surgical procedure might entail. However, in Apr., 1958, the patient's condition had reached such a state that operation was again considered. The patient was hospitalized and angiocardiograms were performed in an effort to determine by what route the systemic blood reached the pulmonary vascular bed. It was the conclusion of the roentgenologist that the pulmonary vessels received most of their blood from the aorta evidently through the bronchial arteries. The pulmonary artery could be seen and measured at least 1 cm. in diameter but had an extremely diminished blood flow.

TABLE 2

PERIPHERAL ARTERIAL OXYGEN SATURATION STUDIES

	Blood Arterial Oxygen Studies		
May 14, 1958:	*Preoperative*		
	Content	*Capacity*	*Saturation*
At rest	19.9	27.0	75%
100% oxygen	21.2		80%
June 4, 1958:	*Postoperative*		
At rest	18.6		86%
Exercise	18.0		83%
100% oxygen	20.2	22.1	94%

Peripheral arterial oxygen saturation at this time showed an arterial oxygen saturation at rest of 75% (Table 2). This was diminished over the arterial oxygen saturation of 1953 when, at the time of cardiac catheterization, it was 84.4% in the brachial artery with a Hgb. of 18.7 Gm. and a hematocrit of 67 (Table 1). With this further evidence of worsening of the patient's condition it was decided that an extracardiac shunt might be helpful.

Therefore, on May 27, 1958, an aortic pulmonary artery shunt, using a Dacron prosthesis, was completed between the left pulmonary artery and the descending thoracic aorta. The prosthetic device used was a woven Dacron DeBakey type of ⅜ in. diameter and approximately 3 to 4 cm. long. On release of the occluding forceps there was obvious improvement in the cyanosis,

FIG. 2

Preoperative chest film. Note that periphery of lung fields are quite clear.

FIG. 3

Postoperative chest film. Vascular markings in the lung field are increased over preoperative state.

not only to the operating team but also to the anesthetist. The heart tolerated the opening to the shunt without any obvious difficulty. The patient's course was relatively smooth and one week postoperatively her arterial oxygen content obtained at the radial artery showed a saturation of 86% and after exercise dropped only to 83% (Table 2). After breathing 100% oxygen the arterial oxygen saturation rose to 94 per cent.

On a follow-up visit in Jan., 1959, 8 months postoperatively, the patient had done remarkably well. Her symptoms were much improved. The Hgb. was 15 Gm. and hematocrit 50 per cent. No phlebotomies had been performed since the operation. Cyanosis had diminished and the conjunctival plethora had lessened considerably. The cardiac findings were essentially the same except for a loud continuous machinery-like murmur heard best over the anterior left chest. X-ray film and fluoroscopic examination of the lungs showed increased vascular markings (Fig. 3).

Comment

This case was of interest from several standpoints. We have presented a case of tricuspid atresia in which the patient has survived to the age of 51, and even had married and been delivered of a normal, although premature child, at age forty-one. During this patient's childhood she was quite ill and could scarcely get about, but during her teens, for some unaccountable reason, her exercise tolerance increased and she was able to carry on in her teens and early adult life considerably better than she had been able to do in her childhood. She finally came to operation because of her progressive downhill course over the last 5 years and laboratory evidence that her peripheral oxygen saturation at rest had dropped from 84.4% to 75 per cent. We speculate that this patient apparently developed sufficient collateral circulation through bronchial arteries to carry on well for 20 to 25 years and then, for some reason, perhaps arteriosclerotic obliteration of these anastomotic channels, the blood flow to her lungs as judged by her clinical course became much less.

At operation the left pulmonary artery was small and the pressure within this artery appeared by palpation to be much diminished. Numerous large collateral bronchial arteries were seen around the pulmonary hilum. A sufficient length of the pulmonary artery was cleaned of surrounding tissue, care being taken not to interrupt the larger of the bronchial arteries; and because of the decision to disturb the collateral circulation as little as possible, it appeared easier to put in a Dacron prosthesis between aorta and pulmonary artery rather than to attempt a direct anastomosis between the aorta and the pulmonary artery. It was for this reason that a woven Dacron tube was sutured first to the pulmonary artery and then to the aorta just below the subclavian take-off. On release of the clamps there was a marked thrill in the pulmonary artery as was expected. We feared that the creation of such a large shunt might have some adverse effect on the heart. However, upon release of the clamps the patient immediately became pinker—this was noted by both the anesthetist and myself—and there appeared to be no immediate adverse effect upon the cardiopulmonary system. After several minutes of observation it was apparent that the patient tolerated the shunt well, and her course for the past 12 months has been most gratifying.

We hope that our experience with this patient will encourage others to take a more hopeful view of some of these patients in an age group in which surgery is ordinarily not considered. Despite our considerable misgivings about the outcome this patient has done remarkably well to date. We will, of course, follow her course very closely.

Pleuropulmonary Tularemia*

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Tularemia is still with us in the South. Since the laiety is aware of the disease in sick rabbits, this vector has become less prominent. Therefore the physician must be aware of the not infrequent tick-borne variety and suspect it in cases of the type described in this paper.

FOLLOWING McCOY'S[1] DISCOVERY and identification of *Pasteurella tularensis,* in 1912, as the agent responsible for a plague-like illness of rodents in Tulare County, California, Wherry and Lamb[2] reported the first human infection by this microorganism in 1914. Since that time thousands of cases have been reported from throughout the world.

Association of the disease with rodents, particularly rabbits, has become common knowledge among laymen and may be a partial explanation for the decreased incidence observed since 1947, when 1,401 cases were reported whereas only 522 cases were recorded in 1956 by the Bureau of Vital Statistics. Thus, avoidance of animals infected with *Past. tularensis* may be largely responsible for reduction in morbidity due to this disease.

Since the report by Francis[3] in 1921, however, it has been recognized that many arthropods may transmit *Past. tularensis* to humans as well as maintain the organism in nature through many generations by transovarian passage. In the Southern United States wood ticks *(Dermacentor andersoni),* dog ticks *(D. variabilis),* and perhaps lone star ticks *(Amblyomma americanum)* are the principle arthropod offenders. In this regard, it is of interest that ticks have been implicated as the vector in a high percentage of cases in several recent reports. For instance, Corwin[4] noted that 28 of 44 cases were related to tick bites. Similarly Callaway[5] reported tick bites accounted for 69% of cases of tularemia seen in southwest Missouri from 1947 to 1951. Giddens[6] has also published an impressive but somewhat lower incidence of tick bites as the only source of infection in 31% of patients with tularemia in Shreveport, Louisiana. With increasing public awareness of the danger of handling wild rodents the incidence of tularemia should fall in years to come, but infection from arthropods will undoubtedly maintain a low level of prevalence since transmission via this route is extremely difficult to control.

Disease in man resulting from infection by *Past. tularensis* may result in a variety of clinical forms generally classified, in order of frequency, as ulceroglandular, oculoglandular, typhoidal and pneumonic. Pneumonia may occur as a part of the other types of infection or may appear as a primary process. To the clinician in practice, recognition of classical ulceroglandular tularemia presents no serious difficulty since a history of contact with rabbits or of insect bite can usually be obtained. On the other hand, typhoidal and pneumonic tularemia cause considerable diagnostic difficulty since the portal of infection is usually not apparent. Although a mortality rate as high as 47% was reported in pulmonic tularemia prior to the availability of streptomycin, there has been a gratifying fall in deaths from all forms of tularemia since 1947, when 58 were reported as compared to 4 deaths reported in 1956. Because of difficulty in making a correct diagnosis of typhoidal or pulmonary tularemia, and because of the high mortality rate attending improperly treated cases, it is worthwhile to re-emphasize certain features of these types of infection. This will be done by citing experiences from 10 cases of tularemia recognized on the wards of the University Hospital and Jackson Veterans Hospital from July, 1955, to July, 1958.

The surprisingly high prevalence of pul-

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monary involvement in 7 of 10 patients (Table 1) was probably fortuitous and reflects the severity of illness at the time of hospitalization. X-ray studies of the chest were made on all 10 patients when admitted to the hospital. Although symptoms of pneumonia were prominent in 5 of the 7 cases, physical signs of pulmonary infection were present in all 7 patients. It may be seen that of the 7 patients with pneumonia, 3 had the ulceroglandular type of infection. Four other patients with pneumonia presented a confusing clinical picture with delirium as the most striking feature. The infection appeared to be cryptogenic in the latter group although contact with a diseased rabbit was subsequently confirmed in one instance. Delirium and azotemia occurred in one patient with ulceroglandular tularemia complicated by pleuropulmonary involvement. An erythematous maculopapular rash was encountered in 2 patients and was so extensive in one instance that a rickettsial infection was considered more likely initially than tularemia. Jaundice was recognized on only one occasion in a patient with pneumonia. Contact with rabbits was the source of infection in 5 cases, tick bites were implicated in 3 instances and the source of infection in 2 cases was not known.

The 3 case reports included below illustrate various therapeutic and diagnostic problems encountered in patients with pleuropulmonary tularemia.

Case Reports

Case 1. A 72 year old farmer was admitted to the Urological Service of the University Hospital on Feb. 4, 1958, because of urinary retention and azotemia of 4 days duration. About 7 days before admission he became acutely ill with chills, fever, cough, nausea and vomiting for which he was admitted to a local hospital. There he was found to be disoriented and an accurate history could not be obtained. A diagnosis of bronchopneumonia was made and therapy with penicillin and streptomycin instituted. Although there was a fall in the height of fever, he did not improve symptomatically. With worsening of mental confusion therapy was changed to a broad spectrum antibiotic after treatment for 2 days with penicillin and streptomycin. The following day urinary retention developed and the blood N.P.N. was found to be elevated. Despite an adequate urinary output via an indwelling catheter, azotemia increased and the patient became more stuporous. Referral to the University Hospital was made when it was apparent his condition was deteriorating despite treatment.

TABLE 1

INCIDENCE OF PULMONARY INVOLVEMENT IN ALL CASES OF TULAREMIA
1955-1958

	Total	*With Pleuropulmonary Involvement*	*Without Pleuropulmonary Involvement*
Ulceroglandular	6	3	3
Typhoidal	4	4	0
Totals	10	7	3

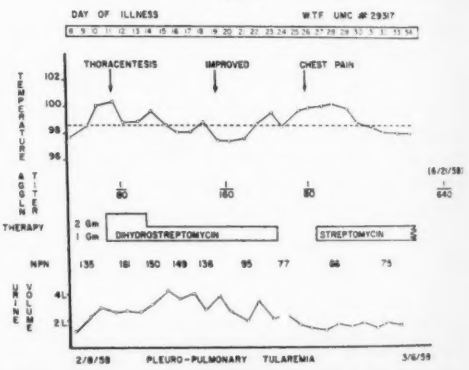
At the time of admission (Fig. 1) he was quite confused and unable to supply reliable information. The B.P. was 160/80, R. 22, and oral T. 98.6° F. He appeared chronically ill but no lesions of the skin or enlargement of lymph nodes was noted. No ulcerative lesions of the eyes, ears, nose, mouth and pharynx were found. The lungs were clear to percussion and auscultation. A grade I systolic murmur was heard at the cardiac apex and the rhythm was sinus. Moderate abdominal distention was present but bowel sounds were active. There was mild generalized abdominal tenderness but no organs could be palpated. An indwelling catheter functioned adequately. Neurologic examination was normal aside from clouding of the sensorium.

X-ray examination of the abdomen on the day of admission revealed marked gastric dilation but no evidence of ileus. Gastric aspiration reduced the abdominal distention promptly. Admission blood studies revealed 12.7 Gm. Hgb. with a PCV. of 39%; a WBC of 8,400 with a differential of 73% neutrophils, 8% band forms, 14% lymphocytes, 2% monocytes and 3% eosinophils. Urinalysis was within normal limits.

On the day after admission his condition was unchanged. Blood chemistry studies revealed a N.P.N. of 135 mg. per 100 cc., with chlorides of 90, carbon dioxide of 15, potassium of 3.9, and sodium of 134 mEq./L. An x-ray of the chest revealed diffuse haziness overyling the entire right lung but the left lung was entirely clear. Hydration was maintained with intravenous isotonic saline and 5% dextrose but no specific therapy was instituted.

Reappraisal of the patient on the 3rd hospital day revealed an ulcer 1 cm. in diameter on the third knuckle of the left hand with palpable and slightly

FIG. 1



Clinical record of a 72 year old farmer with tularemic pneumonia complicating ulceroglandular tularemia.

tender lymph nodes in the left epitrochlear and axillary regions. The percussion note over the right chest posteriorly was dull and breath sounds were distant over this area. Moist rales were audible over both sides of the chest. A thoracentesis on the right side yielded 400 ml. of turbid yellow fluid which clotted promptly. *(Past. tularensis* was subsequently isolated from mice inoculated with this material.) Cultures of blood and sputum were negative for tularemia.

On the basis of clinical and laboratory findings, the diagnosis of *ulceroglandular tularemia with pleuropulmonary involvement* was made. Treatment was begun with dihydrostreptomycin, 2 Gm. daily intramuscularly in divided doses. Blood obtained at this time was subsequently found to have an agglutination titer of 1:80 to tularemia.

Over the ensuing 7 days progressive clearing of the sensorium accompanied rapid healing of the lesion on the hand. The patient was then able to recall having handled a rabbit brought in by a sedentary dog several days prior to the onset of symptoms. However, azotemia persisted despite a high urinary output and required vigorous replacement of fluid and electrolyte. No evidence was found of excessive electrolyte loss in the urine.

Dihydrostreptomycin was continued, 1 Gm. daily, for a total of 14 days. Progressive improvement of the patient's condition with clearing of the sensorium, gradual reduction in azotemia and a normal temperature indicated an adequate response to therapy. A chest x-ray at the time dihydrostreptomycin was discontinued revealed almost complete clearing of the right lung whereas the left lung remained clear.

Three days after dihydrostreptomycin had been discontinued, 18 days after admission, he developed a sharp pain in the left side of the chest worsened by respiration and associated with a nonproductive cough. There was also a modest elevation of T. to 100° F. At the same time, tenderness and swelling of the left calf was found; a venous "cut-down" had been placed in the left foot on admission but had been removed several days earlier. An x-ray of the chest revealed haziness above the left diaphragm with blunting of the left costophrenic angle whereas the right lung appeared clear. An EKG was unchanged with no evidence of right ventricular strain. Although pulmonary embolization was considered a possibility, recurrent pulmonary tularemia was considered more likely. Accordingly, treatment with streptomycin, 1 Gm. daily intramuscularly, was reinstituted with prompt symptomatic improvement and return of temperature to normal levels. Urinary retention persisted due to benign prostatic hypertrophy necessitating continuous bladder drainage by indwelling catheter. Although moderately azotemic, the patient was discharged, fully ambulatory, on the 26th hospital day.

Fourteen days of additional therapy with streptomycin was administered by his private physician for a total of 21 days retreatment. On completion of therapy at home he did well despite moderately severe asthenia still present 4 months after discharge from the hospital. An agglutination test at that time revealed a tularemia titer of 1:640.

Comment. Lack of an adequate history and predominance of symptoms related to the urinary system caused the diagnostic ulceration on the hand and enlargement of the epitrochlear and axillary nodes to be overlooked during the first few days of illness. The extreme elevation of blood N.P.N. levels despite adequate urine flow suggested tubular damage of the type referred to by Giddens[6] although oliguria was not recorded. Symptomatic improvement occurred rapidly after treatment with streptomycin was begun but azotemia persisted for some time before returning toward normal levels. Although a relapse was not substantiated bacteriologically, prompt response to streptomycin suggested that such might have been the case. Similarly, pulmonary infarction was not excluded but absence of hemoptysis, a stable electrocardiogram and the character of the radiographic findings were felt to be against such a diagnosis.

Case 2. A 43 year old welder was admitted to the medical service of the Veterans Hospital on May 28, 1958, because of fever, nausea and vomiting, headache and confusion of 6 days duration. Two days prior to admission he developed a nonproductive cough but there was no pain in the chest. No history of contact with rodents could be obtained from either the patient or his family.

Examination (Fig. 2) revealed a T. of 103° F., B.P. of 110/70 and R. of 22. He appeared well nourished but acutely ill and was obviously confused although cooperative. Numerous healed pigmented scars were found over the upper thorax, hands, arms and face but no ulcers were noted. No enlargement of lymph nodes was detected. The eyes, ears, nose and throat were negative. Dullness to percussion was found over the right lung base posteriorly below the level of the

FIG. 2

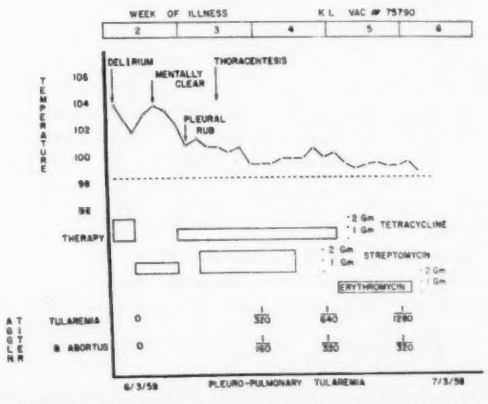


Chart shows hospital course of a 43 year old welder with typhoidal tularemia complicated by pneumonia.

scapula with reduction in the intensity of breath sounds. Crepitant rales were present over both lung bases posteriorly; most marked on the right side. The heart was not enlarged and no murmurs were detected. Moderate abdominal distention with a tympanitic percussion note was noted without evidence of a fluid wave or shifting dullness. No abdominal viscera or masses were felt. Neurologic examination was entirely normal aside from delirium.

Urinalysis on admission revealed a 3+ albuminuria, many hyaline and granular casts but no cells. The Hgb. was 14.5 Gm., hematocrit 45%, WBC 11,800 with 53% neutrophils, 31% band forms and 15% lymphocytes. The VDRL test for syphilis was negative. An x-ray of the chest revealed an area of infiltration at the base of the right lung interpreted as "pneumonitis." Physiologic pressures and dynamics were found at lumbar puncture with a cell count of 2 neutrophils and normal values for sugar and protein. Sputum smears and cultures revealed a normal flora and blood cultures were negative; no effort was made, however, to isolate *Past. tularensis* on special bacteriologic media.

A specific etiologic diagnosis could not be made but the patient was thought to have either a viral or rickettsial infection with tularemic pneumonia, a distinct possibility. Therapy was begun with tetracycline, 2 Gm. daily by mouth in divided doses.

On the 3rd hospital day streptomycin, 2 Gm. daily intramuscularly in divided doses, was substituted for tetracycline because of persistence of fever and mental confusion. By the 3rd day of streptomycin therapy, the 5th hospital day, there was definite clearing of the sensorium despite daily elevations of temperature to as high as 104° F. Tetracycline, 1 Gm. daily in divided doses by mouth, was then restarted on the 7th hospital day and streptomycin, after a lapse of one day, was increased to 2 Gm. daily on the 9th hospital day.

On the 8th hospital day, despite evidence of improvement, a pleural friction rub was noted over the right lung base laterally and was accompanied by physical findings of parenchymal consolidation. An x-ray of the chest revealed increased haziness at the right base with clouding of the costophrenic angle. A diagnostic thoracentesis on the 10th hospital day yielded 10 ml. of yellowish turbid fluid containing 3,000 leukocytes of which 60% were lymphocytes. Cultures of the fluid were sterile but no effort was made to cultivate *Past. tularensis*. As may be seen (Fig. 2) combined tetracycline and streptomycin therapy was continued until the 20th hospital day when streptomycin was discontinued. Tetracycline was continued for an additional 4 days. Throughout this time the patient improved rapidly with complete clearing of the sensorium, increased appetite and improved strength.

Because of persistent low-grade fever, erythromycin was given empirically for 7 days but there was no evidence that the patient's course was altered. The final x-ray of the chest taken on the 24th hospital day showed considerable clearing of the infiltration at the right base.

Of considerable interest was the change in titer of agglutinating antibody to *Brucella abortus* and *Past. tularensis* as depicted in figure 2. Increases in titer to both antigens caused concern that this illness might represent brucellosis. The last determination showed an additional rise in tularemia antibody to 1:1280 whereas the *Br. abortus* titer remained stable at 1:320.

The patient was discharged on the 30th hospital day fully ambulatory and free of symptoms. On this date he recalled for the first time that he had butchered a sick rabbit about 3 days before onset of symptoms.

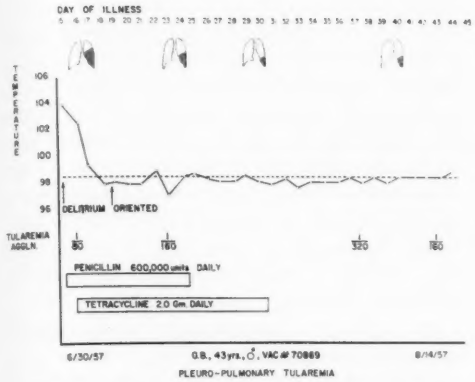
Comment. The patient's illness was typical of typhoidal tularemia with pulmonary involvement the striking physical manifestation. Response to antimicrobial therapy was somewhat slower than is usually seen since low-grade fever persisted for 4 weeks, although striking symptomatic improvement promptly followed initiation of appropriate drugs. The simultaneous rise of agglutinins for *Br. abortus* and *Past. tularensis* has been observed previously and apparently is a nonspecific phenomenon since there is no evidence of a common antigen shared by the two organisms.[20] As in this instance, when no primary ulcer was demonstrated, the higher titer of tularemia antibody should aid in the final differentiation of the two diseases.

Case 3. A 43 year old farmer was admitted to the medical service of the Veterans Hospital on June 30, 1957, because of cough, chills and fever of 2 weeks duration. At the time of admission the patient could give no history because of mental confusion but the following facts were obtained retrospectively. At the onset of illness he was told he had pneumonia and was treated with an unknown amount of oral penicillin for 8 days. There was no evidence of response since fever continued to spike daily to 104° F. and 2 days before admission he became delirious. No history of handling rodents was obtained, although a pet cat had brought in a dead rabbit about 2 weeks before onset of symptoms. Numerous tick bites had been sustained prior to the present illness but no ulcerative lesions or enlargement of lymph nodes had been noted.

Examination (Fig. 3) revealed an acutely ill disoriented man with a T. of 102.4° F., P. 130, and B.P. of 120/80. He was well developed and nourished and coughed frequently during examination. The skin was clear and no lymphadenopathy or tenderness was detected. The eyes, ears, nose, mouth and pharynx were negative. Percussion revealed dullness over the left lung base posteriorly with extension into the left lower axillary area. Breath sounds were diminished in intensity over this area but no rales or friction rub were encountered. The heart was not enlarged to percussion; the rhythm was sinus and no murmurs were heard. Abdominal examination revealed no tenderness, visceral enlargement or evidence of free fluid. There was no cyanosis or edema. Neurologic examination was not remarkable except for the delirium.

Laboratory studies revealed an admission hematocrit of 40%, WBC of 11,250 with 79% neutrophils, 3%

FIG. 3



Record of a 43 year old farmer's illness with pulmonic tularemia complicating the typhoidal form of the disease.

band forms, 17% lymphocytes and 1% monocytes. The urine specific gravity was 1.014 with albumin 1+, sugar negative and many granular casts on microscopic study. The admission BUN. was 17.4 mg. The VDRL test of syphilis was negative. A lumbar puncture revealed normal spinal fluid pressures, 49 mg. of sugar, 28 mg. of protein per 100 cc., and a negative serologic test for syphilis.

Treatment with 300,000 units aqueous procaine penicillin intramuscularly twice daily was begun on the day of admission. Sputum cultures reported on this date were negative; agglutination for *Br. abortus* was negative but tularemia was positive in a titer of 1:80 (Fig. 3). Tetracycline, 2 Gm. daily, in divided doses by mouth, was then added to the therapy. A dramatic decline in temperature occurred on the following day, the 3rd hospital day, and the patient improved mentally. Thereafter he recovered steadily with progressive clearing of the pulmonary infiltration visible on x-ray. Penicillin was discontinued on the 10th hospital day and tetracycline on the 17th hospital day after a total of 14 days treatment. Serum agglutinin titers to tularemia showed rises of 1:160 on the 9th and 1:320 on the 24th hospital day. No effort was made to isolate *Past. tularensis* by culture. At the time of discharge after 31 days of hospitalization, he was free of symptoms.

Comment. In this instance tularemic pneumonia was mistakenly treated as bacterial pneumonia prior to hospitalization. Failure to respond to penicillin after 48 hours of treatment should have provided an important clue to the physician, even though there was no superficial evidence suggestive of tularemia. Therapy with tetracycline was highly gratifying and the rise in agglutinating antibodies confirmed the clinical diagnosis.

Discussion

The cases of tularemia observed in this series serve to re-emphasize the seriousness of such infection and the need for early recognition and prompt treatment. Arthropod borne tularemia continues as a significant route of infection and may become increasingly so as public awareness of the dangers of handling wild rabbits become more widespread. Either mode of infection may present any of the clinical forms of tularemia. The typhoidal form, with or without pleuropulmonary involvement has the gravest prognosis and is the most difficult to diagnose. In only one of the cases of this group with pneumonia was tularemia the initial diagnostic impression. Frequently it was not even considered until late in the disease when the patient's condition had become extremely grave.

Although it has been demonstrated that *Past. tularensis* can penetrate unbroken skin or intact membrane of the gastrointestinal tract, the usual route of entry is through a break in the surface of epithelium.[8] Once beneath the integument proliferating organisms may, but not always, produce a lesion characterized by necrosis and infiltration with mononuclear and polymorphonuclear leukocytes. In either case spread by way of lymphatics to draining lymph nodes then ensues with development of nodal swelling, acute inflammation, necrosis and caseation. From the lymphatic system organisms enter the blood stream and are disseminated throughout the body. It is by such means that remote abscesses develop after a bacteremic episode. Since bacteremia may occur repeatedly in chronic infections with *Past. tularensis*, secondary abscesses may differ not only in size and age but in microscopic appearance. Involvement of the lungs by way of the blood stream therefore is to be expected, usually in the form of confluent lobular pneumonia with considerable involvement of interstitial tissue. Exudate found in alveoli consists predominantly of mononuclear cells. Thrombosed blood vessels are commonly encountered and have been suggested as a contributing factor to the formation of necrotic foci found either in the substance of lung or in pleural space. Pneumonia with abscess formation may be limited to one lung or it may involve all lobes of both lungs.[9,10]

Although this organism was recognized as a facultative intracellular parasite for some time,

the importance of such tropism in the pathogenesis of infection was not appreciated until fairly recently.[11] Intracellular survival for long periods of time in man is a distinct possibility yet has never been demonstrated. Undoubtedly the intracellular location is responsible for destructive lesions found with infection but there has been difficulty in isolating the organism from chronic lesions associated with progressive death of tissue. In this regard, it is of interest that *Past. tularensis* has not been found to produce significant amounts of either exotoxin or endotoxin which might explain certain clinical manifestations of the disease.

As demonstrated by cases of this series, there are no characteristic clinical features of tularemic pneumonia; it is less abrupt in onset than pneumococcal pneumonia and frequently difficult to date precisely as to time of onset. Chill and fever usually occur and are associated with an extreme degree of prostration. Although delirium is most frequently encountered in the typhoidal form of the disease, mental confusion is commonly seen whenever pneumonia complicates ulceroglandular tularemia. A relative bradycardia may be present but peripheral vascular collapse, as occurs with infection caused by other gram-negative organisms, is uncommon. Acute renal insufficiency with oliguria and azotemia has been reported as a terminal complication in 6 of 11 fatal cases reported from Louisiana;[6] a complication not mentioned prominently in the past. The course of typhoidal and pneumonic tularemia may be further complicated by pericarditis and involvement of the central nervous system in the form of peripheral neuritis, encephalopathy, or meningitis.[12]

The earliest roentgenologic manifestation of tularemic pneumonia has been peribronchial infiltration with or without hilar adenopathy. Later as bilateral parenchymal involvement developed, pleural effusion has been a frequent complication.[13] Occasionally nodular densities have been noted but large oval areas of infiltration have recently been suggested as of peculiar diagnostic significance.[14] Generally, however, there have been no specific radiologic changes sufficiently distinctive to permit presumptive diagnoses. As a result, tularemia has been confused with either bacterial, tuberculous or viral pneumonia. Pulmonary infiltrations demonstrated by x-ray have required more time for resolution than indicated by clinical progress. Areas of increased density without detectable effusion or abscess have persisted for several months after clinical recovery. Eventually complete clearing has occurred in uncomplicated cases.[15]

Four of 7 patients with pneumonia in this group developed pleural effusion during their illness; the parenchymal infiltration of one patient appeared nodular; another patient had a large infiltration somewhat oval and well circumscribed in appearance. In no instance did the radiologists suggest tularemia as a possible diagnosis from the x-ray findings.

An elevated sedimentation rate has been an invariable finding but peripheral white blood cell counts have not been consistently elevated. The anemia found after protracted illness has not been notable early in the disease. Studies of serum electrolytes have not been abnormal unless serious complications such as acute anuria have occurred. Jaundice, often noted in patients ill with pneumonia, has been unexplained since a consistent derangement of hepatic function or acute hemolytic mechanisms have not been found. Similarly, no diagnostic urinary changes have occurred although albuminuria has commonly accompanied fever.

Isolation of the organism has been accomplished either by cultivation on laboratory media enriched with cystine or by animal inoculation. It should be emphasized that cultivation of these organisms is a hazardous undertaking since laboratory infections have been common. Personnel engaged in such work should be immunized to minimize risk of infection. Efforts to recover *Past. tularensis* from clinical material should be undertaken before instituting therapy since, as shown by Hunt,[16] the organism is killed rapidly *in vivo* by streptomycin. Thus, cultures obtained from patients treated previously with antibiotics may often be negative.

Agglutinating antibodies have been detected as early as the second week of illness but may be delayed in appearance until the third or as late as the sixth week of illness. This test, therefore, is of limited value when dealing with acutely ill patients early in the disease. Hunt[16] has pointed out that antimicrobial therapy does not retard or depress antibody formation; such has occurred in early treatment of rickettsial infections. A rise in ag-

glutinins later in the disease or after therapy has been effective may provide final proof of a sound clinical diagnosis. Foshay[17] has advocated a skin test with killed bacteria injected intracutaneously; the delayed reaction is read in 48 hours. In his hands, 92% of patients with tularemia had positive tests within the first week of illness. The test was not used in this series of cases.

Hunt[16] advocated a therapeutic trial of streptomycin in cases of undiagnosed pneumonia suspected of either viral or rickettsial origin, when conventional therapy had proved ineffective after 48 hours and when tularemia could not be excluded. The response of tularemic pneumonia to streptomycin was dramatic in most instances since marked symptomatic improvement resulted within 12 to 36 hours after institution of therapy. Although fever fell less rapidly, such management was believed lifesaving in certain instances. Other clinical records have demonstrated the effectiveness of several broad spectrum agents in controlling tularemia, particularly chloromycetin and the tetracyclines. Recent experiments on volunteers, however, have confirmed the superiority of streptomycin as the drug of choice in bringing induced disease under rapid control, as well as providing the best prophylaxis against infection.[18]

Streptomycin alone or in combination with chloramphenicol was used in 9 of 10 patients without a failure. Frequently streptomycin was administered several days after therapy with a broad spectrum antibiotic had been in progress and in such instances appeared to precipitate a change for the better. It should be emphasized, however, that a fall in fever may not be observed for several days after starting treatment with streptomycin and occasionally low-grade fever may persist for several weeks.

No rigid criteria exist for the ideal dosage of streptomycin or the optimum length of therapy. No less than 1 Gm. daily intramuscularly is regarded the minimum adult requirement whereas 2 Gm. daily should cover almost all situations except perhaps dire emergencies. It has been recommended that streptomycin treatment be continued until the patient has been free of fever for 5 days. Others have recommended at least 12 to 14 days of treatment to prevent recurrences. This scheme of therapy is probably ideal since it has been proved repeatedly by clinical trial. Recent studies by McCrum[18] and co-workers demonstrated the specificity of streptomycin in clearing *Past. tularensis* from experimental lesions in man whereas proliferation of the organisms occurred when chloramphenicol was used. If on the other hand either chloramphenicol or tetracycline is selected, 3 to 4 Gm. daily in divided doses for 3 or 4 days or until a response has been obtained should be adequate to bring the infection under control. Therapy can then be reduced to 1.5 to 2 Gm. daily for 12 to 14 days. Risk of relapse following treatment with broad spectrum drugs is appreciably greater than after streptomycin therapy and should be suspected in the event of return of fever.

Immunity to the disease is almost always uniformly solid but reinfection without serious illness can occur since well-documented cases have been recorded.[19] In such instances the infection was mild. In the event of reinfection or relapse, streptomycin has proved effective since there has been no evidence of bacterial resistance.

Summary

Despite striking reductions in reported incidence and mortality, tularemia is and will continue to be a serious infectious disease. Certain diagnostic and therapeutic problems encountered in patients with pleuropulmonary tularemia have been reviewed. Three case reports of pleuropulmonary infection were included to exemplify the difficulties management of this disease may present. It has been emphasized that when confronted with an obscure pulmonary infection, the clinician must always be alert to the possibility of cryptogenic tularemia, since it often presents no distinctive clinical manifestations and laboratory studies are frequently not helpful early in the disease. The rationale for a therapeutic trial of streptomycin in such instances has been reemphasized since it may prove to be lifesaving in critically ill patients.

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Discussion (Abstract)

Dr. Harry E. Dascomb, New Orleans, La. Dr. Allison has expertly re-acquainted us with the epidemiology, protean-clinical aspects, pathogenesis, diagnosis and therapy of tularemia. We in New Orleans wish to thank him for presenting his paper here, since Dr. George W. McCoy, who discovered and identified *Past. tularensis* as the cause of a plague-like disease of rodents was Professor of Preventive Medicine at L.S.U. from 1938 through 1952. Dr. McCoy named the disease *tularemia* after Tulare county in California. This county was named for a variety of bulrush that prevailed in that area and was called "Tule."

Tularemia is endemic throughout the United States and particularly in the South. It is a severe infection that may become chronic and demands early diagnosis and specific therapy to reduce further mortality and hasten convalescence. The clinical diagnosis is difficult in 30 to 40% of the cases because of the wide variety of clinical syndromes that *Past. tularensis* may produce. The clinical picture is determined by the portal of entry of the parasite, the host resistance and the duration of illness prior to examination. Thus, invasion through the skin may result in a local lesion and associated lymphadenitis. In south Louisiana, contact with infected rabbits results in overt hand lesions, while in north Louisiana, Arkansas and Missouri, the primary lesions are frequently arthropod-borne and hidden in body folds. Recently, we saw an elderly man with fever, interstitial pneumonitis, clouded sensorium, who attributed a right inguinal mass to a hernia. Later, a large ulcer was found medially beneath the right gluteal fold and only then did the patient recall being bitten by a tick. Diagnosis of tularemia was confirmed by the agglutination titer of 1:1280 against *Past. tularensis* and streptomycin therapy resulted in satisfactory convalescence. Occasionally, the parasite enters unbroken skin causing no ulcer. This phenomenon was demonstrated by Hachira Ohara in 1925 in a very crucial experiment. He applied infected rabbit tissue to the skin of his wife's hand. Two days later she noticed axillary adenitis. Fever and other signs of infection appeared 4 days after inoculation. *Past. tularensis* was recovered from axillary glands 18 days after her exposure. Typhoid-like disease or primary pneumonia result when *Past. tularensis* is ingested or inhaled.

The human host's resistance tends to limit the initial infection to the lymphatics. Absence of resistance permits the bacteria to filter through the lymphatics into the blood and infect the reticuloendothelial cell system. In this manner, the clinical manifestations vary according to the degree of localization in the lungs, spleen, liver, bone marrow and serosal surfaces of lungs, heart and central nervous system. Jaundice that is occasionally seen is a manifestation of severe illness. Verbrycke and later Francis described miliary areas of necrosis and cloudy swelling of sufficient degree to cause jaundice. Cloudy swelling alone may cause hepatocellular dysfunction as shown by Zimmerman and Thomas in a study of pneumococcal pneumonia.

Although there are no pharmacologically active endo- or exotoxins derived from *Past. tularensis*, certain aspects of the disease as it progresses suggest a host reaction to the breakdown products of the parasite. For example, the generalized erythematous rash that occurs in an occasional case appears 14 days or more after the onset of disease when bacteremia cannot be demonstrated. Indeed, no bacteria are found in the lesions by direct stain or culture. This skin eruption has erythema, multiforme characteristics such as macules, papules, nodules, vesicles and urticarial wheals. These involve the upper trunk and extremities and are particularly numerous in the area of lymphatic drainage of the primary lesion. Microscopically, the lesion consists of lymphocytes and epithelioid cells that are perivascular. In 1950, Dr. Allison and I saw a middle-aged woman with ulceroglandular disease in the 16th day of her illness. Streptomycin was begun; 12 hours later, papules appeared on her trunk and extremities. I am not aware of any attempts to detect tularemia and antigen in such lesions. A study applying Carl Larson's precipitin technic as well as careful bacteriologic studies might help explain the pathogenesis of the skin lesions and other apparent nonbacterial reactions in the kidney and brain.

I agree with the therapy recommended by Dr. Allison. Streptomycin is the most bactericidal of the effective antibiotics and is the drug of choice. Since convalescence depends ultimately on the host defenses, therapy must be prolonged until these appear. Serologic response of the patients with infectious disease depends on the mass of antigen released in the body by the pathogen. The experiences of Smadel,

Larson, and McCrumb strengthen this concept. In most cases, as reported by Hunt, therapy of tularemia is initiated approximately 7 days after onset of illness. Thus, when an antibiotic is continued 5 days after defervescence, approximately 18 days will have elapsed from onset of illness. During this time sufficient antigenic stimulation and antibody response will have occurred. However, if therapy is begun earlier, prior to, or early during fever and bacteremia, it is quite likely immune mechanisms may be obviated or delayed. Thus, the earlier therapy is introduced, the longer it should be continued if relapse due to persisting *Past. tularensis* is to be prevented. I would suggest 21 days or less should specific antibodies appear in titer of 1:320 or more.

One of Dr. Allison's cases revealed agglutinins to brucella as well as *Past. tularensis*. This may be an anamnestic rise due to prior brucellosis as suggested by Karl Meyer. However, serum of rabbits previously immunized with either *Past. tularensis or Br. abortus* reveals antibody response to a common protein antigen. Such an antigen would better explain the presence of brucella agglutinins in patients with tularemia and vice versa.

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SMA's 53rd Annual Meeting

Clinical Management of Acute Bronchiolitis in Infants

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The management of this disease has been much easier and with a much better prognosis since the advent of antibiotics and oxygen therapy. With proper treatment the mortality should be nil.

ACUTE BRONCHIOLITIS (interstitial pneumonitis, capillary bronchitis) is one of the important respiratory diseases of infancy. It is characterized by respiratory distress with emphysema which may appear at first to be benign but can progress rapidly with serious consequences. Since it occurs in all areas of the United States, it presents therapeutic problems to all practitioners with young patients.

A typical history concerns an infant with a mild "cold and cough" for several days. Somewhat suddenly he develops acute respiratory distress, accompanied by restlessness and refusal of feedings. Physical examination reveals dyspnea with emphysema and wheezing or fine rales. There may be low-grade fever, mild dehydration and cyanosis.

The progression of the disease is variable. Some cases continue to be mild. Many of the patients, however, soon become critically ill with marked respiratory distress and clinical signs suggesting severe bronchopneumonia and heart failure.

The pathologic lesions consist chiefly of bronchiolitis and interstitial pneumonitis with patchy atelectasis and emphysema. Late cases show infiltration into the alveoli which gives the picture of confluent bronchopenumonia.

The etiology is not fully understood. Trask[1] reported a series of 103 cases of bronchiolitis from which he isolated Pfeiffer's bacillus (*H. influenzae*) in 71 per cent. In some, pneumococci were also present. He called the disease "Pfeiffer's bacillus pneumonia." Liston[2] recovered *H. influenzae* from 95% of 40 autopsies in children with bronchiolitis and bronchopneumonia. There have been other studies from which no single bacterial agent was isolated with regularity. However, *H. influenzae* is a fragile bacterium which can be missed easily unless special attention is paid to its cultivation and identification. During the past few years, we have been inquiring into the etiology of acute bronchiolitis in infants. Bacterial studies agreeably support Trask's findings. From one series of 51 infants[3] 61% yielded *H. influenzae* on culture of nasopharyngeal mucous. From another series of 73 patients *H. influenzae* was recovered from 67 per cent.[4] Pneumococcus was frequently associated with the *H. influenzae* and, in a few cases, was found alone in our cultures.

Circumstantial evidence has long led investigators to believe that the primary infectious agent is viral, but only recently Ward[5] and Chanock[6] were able to identify respiratory viruses which might be associated with the etiology of this disease.

The mortality rate and the course of the illness have been remarkably improved by modern therapeutic measures. In his report on patients studied between 1927 to 1933, before the advent of antibiotics or oxygen therapy, Trask[1] noted that the over-all mortality was 28% with 50% in the 3 month age group. Clinical improvement in survivors was gradual in contrast to the crisis which was usual in pneumococcal pneumonia. Relapses were frequent. During the period of time from October, 1956, through March, 1959, 105 children under 2 years of age have been treated for acute bronchiolitis without a single death from this disease on the Pediatric Ward of Vanderbilt University Hospital. The average stay in the hospital was 7 days. Re-

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lapses occurred but were unusual. Table 1 shows the ages of the patients. It can be seen that 57% were in the 3 month age group while 85% were 6 months or younger.

Treatment

The objective of this present report is to outline and to discuss the therapy employed in the treatment of these patients.

The therapeutic measures to be discussed are divided into three categories:

1. To relieve the hypoxia and respiratory distress.
2. To combat the infections.
3. To provide general supportive measures.

The relief of hypoxia and respiratory distress is of immediate import. These patients do best in an atmosphere of oxygen at 40 to 50 volumes per cent concentration with relative humidity approaching 100% at a temperature of 19 to 20° C. These requirements are seldom met by the usual oxygen tent. We have been fortunate at Vanderbilt in having available for oxygen therapy an open top clear plastic box which has been described by Batson.[7] It greatly facilitates nursing care and fulfills the atmospheric requirements. When oxygen is no longer needed compressed air may be used. We feel strongly that this good equipment has been a major factor in saving many lives. When air hunger is relieved, these restless, dyspneic babies become quiet and usually fall asleep, making the use of sedatives unnecessary.

To combat bacterial infection, chloramphenicol has been found to be the drug of choice. It is administered in doses of 50 to 60 mg. per kilo of body weight per day, preferably intramuscularly in 4 divided doses. When clinical improvement permits, the drug may be given orally, but it should be continued for at least 6 days of total medication. There are other antibiotics which are effective against *H. influenzae*, notably tetracycline. We have found, however, that in critically ill patients, we rely on chloramphenicol as the superior antibiotic. Penicillin may be added to the regimen since it is the drug of choice for pneumococcal infections.

There is no specific therapy available at present for respiratory viral infections. Gamma globulin has been shown to contain antibodies against many of the infections which are common in the population. With the hope that it might be helpful, we elected to test it in some of our sickest young infants. The dosage was empirically chosen at 2 cc. given intramuscularly at one time, 1 cc. in each of two sites. The clinical improvement which followed was so impressive that gamma globulin was added to the therapeutic regimen of the majority of the subsequent patients during a severe epidemic which occurred during the winter of 1956-57. All of the patients recovered. Later, there were published reports which indicated that gamma globulin potentiates the effect of antibiotics when given in combination.[8-10]

Heart failure associated with bronchiolitis is difficult to detect clinically. Tachypnea, widespread rales and tachycardia are part of the usual picture of this disease. The emphysema may mask the cardiac size and flatten the diaphragms making the liver and spleen palpable. When the liver seems actually to be enlarged and not merely displaced, and the heart rate is above 180, digitalization is recommended. A rapid method is employed using either cedilanid or digoxin, given intramuscularly and monitored by electrocardiograms. A total digitalizing dose of 40 to 60 micrograms (0.04-0.06 mg.) per kilo of body weight is used in infants with one-half the estimated dose given at once. The remainder is given in two divided doses at either 3 hour intervals for cedilanid or 6 hour intervals for digoxin. Digitalization is maintained by digoxin, one-eighth the total digitalizing dose given at 12 hour intervals by mouth.

Table 2 lists the various therapeutic regimens for 105 consecutive patients under 2 years old. It can be seen that chloramphenicol was the antibiotic chosen for 83 patients, tetracycline 15, and erythromycin seven. Penicillin was also administered to 6 of these. Gamma globulin was given to 65 in combi-

TABLE 1

AGES OF 105 PATIENTS WITH ACUTE BRONCHIOLITIS ADMITTED TO THE PEDIATRIC WARDS OF VANDERBILT UNIVERSITY HOSPITAL BETWEEN OCTOBER, 1956 AND MARCH, 1959

Age of Patients	*Number of Patients*	*Per Cent of Total*
0-3 months	60	57.2
4-6 months	29	27.6
7-12 months	10	9.5
12-24 months	6	5.7

TABLE 2

THERAPEUTIC REGIMENS OF 105 CONSECUTIVE PATIENTS WITH ACUTE BRONCHIOLITIS TREATED BETWEEN OCTOBER, 1956 AND MARCH, 1959

Chloramphenicol*	1
Chloramphenicol and oxygen	21
Chloramphenicol, oxygen and gamma globulin	61
Tetracycline*	5
Tetracycline and oxygen	6
Tetracycline, oxygen and gamma globulin	4
Erythromycin and oxygen	7
Penicillin added to one of the above regimens	6
Digitalization in addition to one of the above regimens	8

*These patients were placed in the Batson box with moisture and compressed air but no added oxygen.

nation with an antibiotic. Eight patients were digitalized.

The single most important factor in successful care of infants with acute bronchiolitis is careful nursing. These patients require almost constant attention during the first day or two in the hospital. Nasal discharge and crusts may block the airways so that oxygen cannot reach the lungs. Gentle suctioning which is effective yet not traumatic is important. Since the infants become exhausted after taking small amounts of fluids, hydration is difficult to maintain. It has been our experience that an exhausted, dyspneic child will fall asleep once he is comfortable in the oxygen box. He becomes restless with hunger and sleeps again after a small feeding by nipple. He wakes again soon, however, and is easily satisfied with a little more fluid. Gradually he is able to rest and take feedings alternately so there is rarely a need for intravenous fluids or sedatives. A shortage of trained nurses to supply this kind of care is a constant problem. We, therefore, ask the mother to stay with the child. She can be instructed to observe for nasal stuffiness, to feed and to change the diapers while the child is in the oxygen box. Most mothers are good at caring for their own, and we believe the ill, frightened child appreciates the security of her presence.

Regarding sedation, it is well to remember that most of the commonly used sedative drugs may depress respiration and are, therefore, contraindicated in an hypoxic patient. Small doses of chloral hydrate may be used after the child has regained a good color. With the relief of hypoxia, however, the frightened restlessness seems to pass and sedatives are not necessary.

Caution must be exercised, also, in the use of intravenous fluids. With impending heart failure already present, the margin of safety is easily exceeded. Unless the child is markedly dehydrated from vomiting or diarrhea, a conservative approach to hydration is strongly recommended.

Summary

Therapeutic measures for acute bronchiolitis in infants have been described and discussed. These include measures for relief of hypoxia and respiratory distress, combatting the infections, and general support of the patient, including digitalization and special nursing care.

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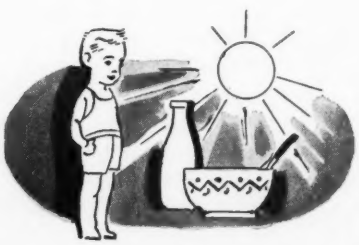

Cytologic Diagnosis of Cervical Malignancy: Routine Smears in Private Practice*

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The authors emphasize the accuracy of cytologic diagnosis as confirmed by adequate cervical biopsy by the knife. They stress the wide conization of the cervix as a proper biopsy to obtain sufficient tissue for pathologic study.

THE VALUE OF EXFOLIATIVE CYTOLOGY for the early detection of cervical cancer has been proven by statistical reports gathered by screening projects and from large medical institutions. The reliability of such a procedure depends, however, on the follow-up of positive or suspicious smears by adequate biopsy and histologic examination of the specimens.

McLaren, Taylor and Atwood,[1] reporting in the Lancet, 1958, have stated that the chief function of cytology is to reveal carcinoma in situ in the clinically normal cervix. Their unexpected pick-up rate was 3.5 per 1,000 patients. We agree with such a statement, but also feel that cytologic examination of vaginal and cervical smears is quite valuable in the diagnosis of unsuspected invasive cervical cancer. Two of our 9 invasive cases were totally unsuspected, and the diagnosis was first discovered by positive smears and later confirmed by biopsy.

Berg and Bader,[2] reporting in Cancer, 1958, after a 6 year study of 2,281 patients, conclude that annual cervical cytologic examination would practically eliminate deaths from cervical cancer. Such an examination was the primary means of detecting 91% of cancers found in their series.

We agree with these authors that, when carried out with the proper technic, the cytologic test is the most accurate method of finding early curable cervical cancer. We must add to this statement, however, that the test is valueless unless its interpretation is done by a competent well-trained cytologist. We do not feel that a good clinical laboratory technician can become a cytologist in 60 to 90 days study. Such a period of time is also inadequate for training a cyto-technician or a "screener." Most authorities feel that certification as a cyto-technician and screener requires one year of training. It usually requires an additional one to two years intensive study to qualify as a competent cytologist. We are thoroughly in agreement with the proposed classification of such personnel into cyto-technicians, cyto-screeners and cytologists. Unquestionably, the lack of such trained personnel has limited greatly the use of this examination.

We have no quarrel concerning the pathologists and their interest or lack of interest in cytology. Those with whom we are in contact have been most cooperative, particularly so since we acquired the services of a competent cytologist before we began the routine use of such a procedure.

The average general practitioner and often the gynecologists are unable to take advantage of this excellent diagnostic aid unless they practice near one of the large medical centers. It will require many years before this test is available to the general population. It is of interest to report, however, that Calabresi, Awold and Stovall[3] of Wisconsin Medical School screened 65,163 women from 1947 to 1956. Many of them were located in rural areas and the smears were made by the local physicians and mailed to the university laboratory. This method is one way of reaching the general population, but requires real teamwork between the physician, cytologist,

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and pathologist. Its main disadvantage seems to be its cost.

During the past 3 years we have been fortunate in having the full-time services of an exceptionally well-trained cytologist in the Department of Gynecology and Obstetrics at the Browne-McHardy Clinic. This report concerns our experience in private practice with routine vaginal and cervical smears for diagnosis of uterine malignancy. The majority of the patients examined cytologically were referred from the Medical Department for a routine pelvic examination. In most instances there had been no gynecologic symptoms.

We feel that the value of vaginal cytology is mainly as a routine test for all women. By means of such examinations many unsuspected intra-epithelial lesions will be discovered at a time when nonradical surgery will be curative. Occasionally an invasive lesion will be found. Its use in women having gynecologic symptoms or gross cervical lesions is of less value as most of these will require additional diagnostic procedures.

From September, 1955, through September, 1958, we have screened 2,594 patients, 29 of whom had positive or suspicious smears. Papanicolaou class III, IV, and V comprised these positive or suspicious smears. In addition, during this same period our cytologist has examined smears made under our supervision from 438 patients registered at the gynecologic clinic, Touro Infirmary. Among this group 16 had positive or suspicious smears.

Errors in diagnosis of carcinoma in situ of the cervix often result from inadequate biopsy. At times such an error may represent a misinterpretation of cellular atypism associated with pregnancy or inflammatory disease. The majority of well-trained cytologists, however, do not agree that associated pregnancy should cause confusion in interpretation of vaginal or cervical smears. There is certainly no doubt that inadequate biopsies often prevent the pathologist from confirming the cytologist's finding of malignant cells. The histologic features of carcinoma in situ of the cervix as repeatedly discussed by many authors[4] are that it is predominantly a lesion of the squamocolumnar junction. Cytologically it mimics cancer, and histologically it involves and is limited to the epithelial surface or endocervical glands without invading the underlying stroma. This description clearly indicates the need of adequate tissue for microscopic examination.

Technic

The technic for obtaining smears is quite simple. It was first suggested by Kernodle, Cuyler and Thomas.[5] We feel that a better smear is obtained by aspiration than by direct scraping. Two smears are made on each patient. A vaginal smear is obtained by introducing the glass pipette into the posterior fornix. Secretions are aspirated, and then blown onto a glass slide. They are then spread thinly with the flat side of the pipette. A cervical smear is obtained, after the speculum, without lubrication, is inserted into the vagina. The pipette is placed in the cervical os and secretions are obtained from this area. The great majority of malignant cells will be found in smears taken from the cervical os.

A third smear is obtained from the endocervical canal after passing a sound into the uterine cavity of patients with a history of irregular or postmenopausal bleeding.

Positive Smears

Our procedure, when positive smears are found, consists of first obtaining additional smears. We then do a deep cold-knife cervical conization to determine if a malignant lesion is present, and if so, whether it is intra-epithelial or invasive. If the lesion is an intra-epithelial one, we advise total hysterectomy unless the patient is under 35 and is desirous of having children. In such cases we feel safe in following them with smears three to four times a year. If subsequent smears become positive we advise hysterectomy without further delay.

Eleven patients were found to have intra-epithelial cancer of the cervix, all unsuspected. Nine of these were treated by total hysterectomy. One patient, age 20, was quite anxious to have children. She received cervical conization only, and has continued to show negative smears 2 years postoperatively. One patient age 76 returned to her former physician and has had, to our present knowledge, conization only.

If the original cervical cone biopsy shows invasive cancer, the patient is treated by irradiation. This consists of deep x-ray, fol-

lowed by intra-uterine and intra-vaginal radium. Nine patients having invasive cervical cancer, two unsuspected, were treated in this manner.

Two patients having endometrial cancer were treated with intra-cavitary radium, followed 6 weeks later by total hysterectomy and bilateral adnexectomy.

We cannot stress too strongly the importance of a deep cold-knife cervical cone biopsy that includes the entire squamo-columnar junction. This is an operating room procedure. There are two points concerning it that we would like to stress. The first is, no vaginal scrubbing is done because of the possibility of removing superficial malignant cells by too vigorous preparation. Secondly, we never use the cautery or coagulator to control bleeding because this could cause cellular changes that would prevent the pathologist from making a satisfactory examination. Bleeding is controlled by sutures or by means of a vaginal pack. Conization of the cervix is then followed by cervical dilatation and curettage of the endometrium.

Statistics

From September, 1955, through September, 1958, we have examined smears, using the Papanicolaou staining technic, from 2,594 patients, in our private practice at the Browne-McHardy Clinic, 29 of whom had positive or suspicious smears (Table 1). One patient refused further examination and was lost. Twenty-eight of these patients had a cervical conization and dilatation and curettage done for confirmation of the cervical smear. Twenty-two of these patients had smears suspicious or positive for cancer of the cervix, 20 being confirmed by cone biopsy. One patient was found to have chronic cervicitis only. No follow-up smears were done as she died 3 months after conization, following a coronary occlusion. The other patient had a class III smear on first examination, and a class II-A on repeat smear. Cone biopsy was reported as showing atypical basal cell hyperplasia. Six patients had smears suspicious or positive for endometrial cancer, 2 being confirmed by curettage. The remaining 4 showed endometrial polyps or hyperplasia of the endometrium.

TABLE 1

INCIDENCE

Suspicious or positive smears	29 of 2,594 patients (1 per 93)
Suspicious or positive for cervical cancer	22 (1 per 118)
Verified by cone biopsy	20 (1 per 120)
Carcinoma in situ	11—all unsuspected (1 per 236)
Invasive cancer	9—2 unsuspected (1 per 1,297)
Unsuspected cervical lesions	13 (1 per 199)
Suspicious or positive for endometrial cancer	6 (1 per 432)
Verified by histologic examination	2 (1 per 1,297)

Our incidence of "unconfirmed positives" was actually one out of 21 patients whose smears had been reported as suspicious or positive for malignancy of the cervix uteri. This compares very favorably with the reports of Counseller,[6] Allan[7] and others. There does not seem to be any universal agreement, however, as to the manner in which such should be interpreted or reported. Up to the present time we are not aware of any "false negatives."

Summary and Conclusions

We have reported our experiences with vaginal cytology at the Browne-McHardy Clinic during the past 3 years. The majority of these examinations have been a part of routine study on women referred from the Medical Department, few of whom had gynecologic symptoms.

We have found 29 suspicious or positive smears in 2,594 patients. Cold-knife cervical conization and dilatation and curettage confirmed the cytologist's report of cervical cancer in 20 of 22 cases. Two of the 6 suspected endometrial cancers were confirmed by histologic study. One patient refused further study.

We cannot emphasize too strongly the importance of a wide and deep cold-knife cervical conization in order to obtain sufficient tissue for the pathologist.

Finally, we feel that vaginal cytology is an essential part of routine examination of all women. Through such means many unsuspected malignant cervical lesions will be discovered at a time when they can be cured.

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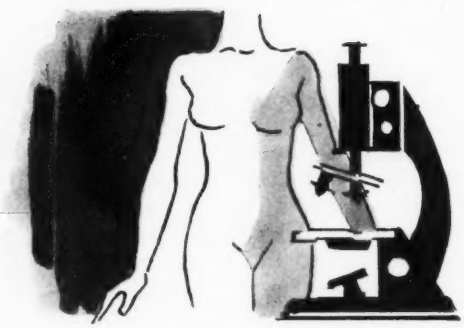
Discussion (Abstract)

Dr. John R. Kight, Norfolk, Va. Concerning the value of exfoliative cytology in the early diagnosis of cervical cancer, the results that can be obtained have been presented often, and no longer is it necessary to defend the place of routine smears in our diagnostic armamentarium. Cervical smears can no longer be considered a "desirable luxury" or a "helpful adjunct" to diagnosis, but are absolutely necessary without which, no physician who professes to examine a woman's pelvis intelligently can be said to be practicing adequately in our present knowledge.

The lack of an available cytologist has often been cited as a hindrance to the employment of routine smears. True, all communities do not have such facilities locally but methods of handling smears by mail have been proved to be perfectly satisfactory. The fact that so many smears must be taken before a positive one is found is an argument used by some who feel that the low yield does not justify the routine employment of the smear. Yet in private practice we find far more positive smears with routine cytology studies than we do new cases of lues with routine serology tests. From results obtained and patient's desire for cancer smears, the gynecologist should be convinced that it is not necessary to debate the cost as a reason for not including this procedure as a routine. A review of the charges of all laboratories in the State of Virginia revealed some variation, but certainly none that were excessive. Where else in medicine can one pay to almost assure one's self against developing a fatal condition? We, the gynecologists, must in an effort toward cancer control, unhesitatingly recommend that all routine pelvic examinations include exfoliative cytology studies and must introduce new ideas that will occasion more frequent examinations of a larger population. A review of the cases treated in De Paul Hospital for carcinoma of the cervix often showed an individual who had been hospitalized during the several years preceding the diagnosis for a condition unrelated to the pelvis. With this in mind, we are now setting up a system where any attending physician can order a vaginal smear on any hospitalized female patient as simply as can be ordered a blood count.

Opinions vary as to the age at which cytologic studies should be included as a routine procedure. Malignancy of the cervix is virtually nonexistent in the teen-aged girl but this is far from true in the 20's. Ferguson and Cavenaugh reported 32% of their positive smears in patients 29 years or younger. Precancerous and invasive lesions are seen too often in the 20 to 30 age group to warrant setting the lower age limit at 30 as suggested by Dr. Johnson and his co-workers. To obtain more far reaching results, I would certainly recommend that those in the 20's be also screened for a possible malignancy.



CASE REPORT

Malignant Meningioma: Case Report of a Parasagittal Meningioma of the Right Cerebral Hemisphere with Multiple Extracranial Metastases to the Vertebrae, Sacrum, Ribs, Clavicle, Lungs, Liver, Left Kidney, Mediastinum and Pancreas*

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Introduction

THE LITERATURE on extracranial metastases of meningiomas has been reviewed recently by Ringsted.[1] His paper contained a table of the 17 cases, including his own, which he considered acceptable examples and which had been reported up to that time (1958). The following case (the eighteenth in the literature) is presented because of its rarity and interest to neurologists, neurosurgeons, and neuropathologists alike.

Case History

A 31 year old white woman was operated upon first in 1942, in another hospital, at which time a circumscribed globular meningioma was removed from the right occipital region. Grossly the tumor was considered to be benign, and the initial microscopic examination likewise was in agreement, though the opinion was later reversed. She did well until 1950, when a sharp and rather constant pain developed in the right side of the face and above the right eye. She had had a persistent left homonymous hemianopsia since the original operation in 1942. A carotid arteriogram in May, 1951, was interpreted as being within normal limits. There was considerable optic atrophy but no evidence of choked discs.

The next admission was in June, 1951, when she was on the Psychiatric Service because of severe headache, weeping, crying, and tearing her hair. She was taken home 24 hours later against advice.

The third admission to the Medical College of Virginia Hospital was on Aug. 23, 1951; she was discharged on Sept. 19, 1951. At that time she had 4 to 5 diopters of choked disc and a recurrent meningioma, "approximately the size of a baseball," was removed from the right occipital region. The microscopic interpretation was recurrent malignant meningioma with invasion of the leptomeninges. It was believed that the adjacent cerebral cortex was probably invaded, though definite cortical tissue was not identifiable.

The fourth admission to the Medical College of Virginia Hospital was on Feb. 3, 1952, when the patient again complained of severe headache. There was a prominent functional component to her symptomatology, in addition to her serious organic intracranial lesion. Roentgenotherapy was given to the supposed remnants of the neoplasm in the right parieto-occipital region.

In the interval between the fourth and fifth admissions, the patient had a left salpingo-oophorectomy and partial resection of the sigmoid colon at another hospital because of a benign thecal cell tumor of the ovary. The sigmoid resection was for technical reasons because of the size of the lesion (13.5 by 21 by 9 cm.).

The fifth and final admission to the Medical College of Virginia Hospital was on Apr. 15, 1955, being precipitated by the development of an acute paraplegia. There was a sensory level at the 8th thoracic dermatome bilaterally, with hyperesthesia above that level. Roentgenograms revealed pathologic fractures of the 7th and 8th thoracic vertebrae with gross destruction of the adjoining laminae and possible mediastinal involvement. No operative procedure was performed and roentgenotherapy produced no appreciable benefit.

The patient never regained any motor power in her legs and expired on Oct. 26, 1955.

During the period of hospitalization, an ulcerative lesion developed on the gingiva, and a mass which appeared to be attached to the left clavicle manifested itself.

The *autopsy* was performed one hour and fifteen

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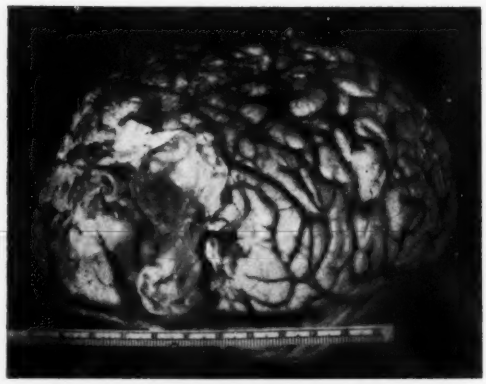
FIG. 1

Photograph of brain with the well-circumscribed tumors in the right parietal and occipital lobes.

minutes after death (A-8870). The body showed evidence of the previously described surgical procedures and only those changes related to the neoplasm are described.

The examination of the brain revealed two tumors which were slightly lobulated, gray-white, and very firm to the point of feeling hard to palpation. The smaller measured 16 mm. in diameter and was in the posterior portion of the right parietal lobe, 1 cm. from the midline superiorly (Fig. 1). The larger replaced the occipital lobe posteriorly and measured 20 by 28 by 34 mm. The tumors compressed the brain and shelled out completely, showing no evidence of invasion of brain tissue or blood vessels (Fig. 2). On cut section, the larger revealed an area of hemorrhage. There was a similarly appearing single nodule in the right lower lobe of the lung (1 cm.), head of the pancreas (3.5 cm.), the lower pole of the left kidney (8.5 cm.), and the right lobe of the liver (2.5 cm.). These were sharply outlined and gray-white, with areas of congestion or

FIG. 2



Same as in figure 1, with the tumors removed revealing the clean base and gross lack of invasion.

FIG. 3

Metastatic tumor in the left kidney. Note the sharp line of demarcation.

hemorrhage. There was slight lobulation and variation in color noted on section, as seen in the kidney (Fig. 3). Less distinctly delineated masses were present in the right sternoclavicular joint, left 8th and right 9th ribs, thoracic and lumbar vertebrae and sacrum. The 7th and 8th dorsal vertebrae were partially collapsed (Fig. 4). The tumors extended from the bones in a number of sites with the lesions producing extra-osseous masses ranging up to 7 cm. in diameter. The larger masses were in the sacral and sternoclavicular regions. In addition to these, there was a 1.2 cm. ulcerative lesion in the gingiva of the left mandible adjacent to the third molar which did not appear to involve the bone.

The original tumor,* removed in 1942, revealed large areas of necrosis histologically, and areas of proliferating connective tissue. The tumor varied from field to field; however, it was essentially similar throughout, having three slight variations. One of these consisted of indistinct whorl-like arrangements of cells separated by distinct vascular channels (Fig. 5). The cells in these areas revealed nuclei which ranged from essentially round to elongated blunt-ended or spindle-shaped structures with finely distributed chromatin material and an occasional distinct nucleolus. The cell outlines were indistinct, and the cytoplasm appeared to be fibrous. These areas appeared to merge almost imperceptibly into more highly cellular foci in which the vascularity appeared to become less and the nuclei larger. The nuclei were more vascular and contained finely dispersed chromatin. In these fields the fibrillar structure of the cytoplasm was less distinct or not visible, and

*The slides of this tumor were made available through the courtesy of Dr. James R. Cash, Department of Pathology, University of Virginia, Charlottesville, Va.

FIG. 4

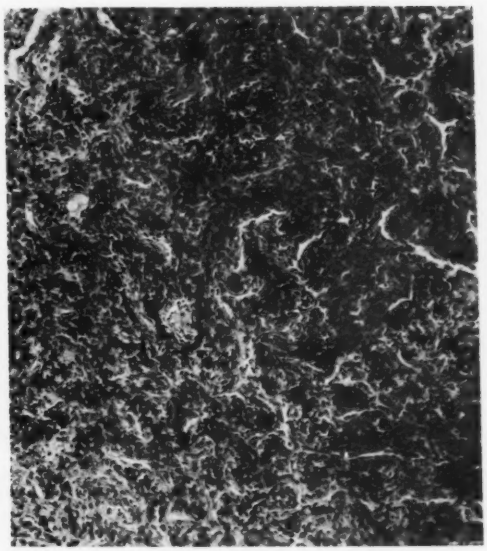
Photograph of 7th and 8th thoracic vertebral bodies with partial collapse and extension of tumor through the cortical portion.

occasional almost solid masses of nuclei were present. A rare mitotic figure was seen within the tumor and they were located in the more highly cellular areas (Fig. 6). The third picture was that of a more compact elongated cell of spindle shape, having a fibrous appearance.

The second tumor, removed surgically in 1951, (Figs. 7 and 8) revealed essentially the same picture as seen in the original specimen of 9 years earlier; again larger areas of necrosis were present. The tumor, although showing all areas previously described, tended to have a larger proportion of the more compact highly cellular areas and less of the vascular pattern noted in the first tumor.

The final tumor removed at autopsy (1955) still maintained a few of the whorl-like arrangements separated by large vascular channels, as noted in the original section (Figs. 9 and 10). This represents the minority of the tumor, since it had become more cellular with a less distinct whorl-like pattern. The nuclei were somewhat more irregular and the chromatin material appeared increased. The whorl or net-like arrangement was still present within the metastasis (Fig. 11) although the more highly cellular

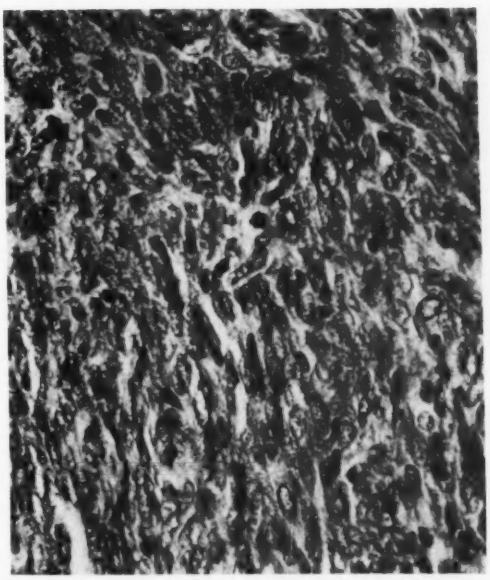
FIG. 5



Photomicrograph of the original surgical specimen (1942) showing the whorl-like arrangement and prominent vascular pattern. (H & E X 130)

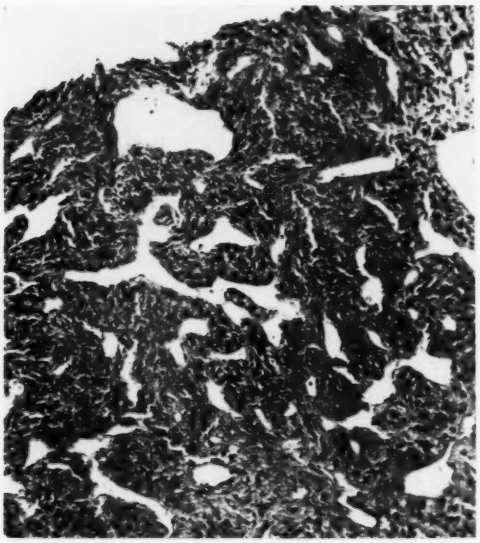
and compact masses tended to dominate the picture. Distinct nucleoli were everywhere in evidence. The cells tended to become larger, the nuclei rounded or

FIG. 6



Taken from the more fibrous portion of the original tumor. Note the mitotic figure near the center. The vascular pattern is still present though less prominent in these areas. (H & E X 400)

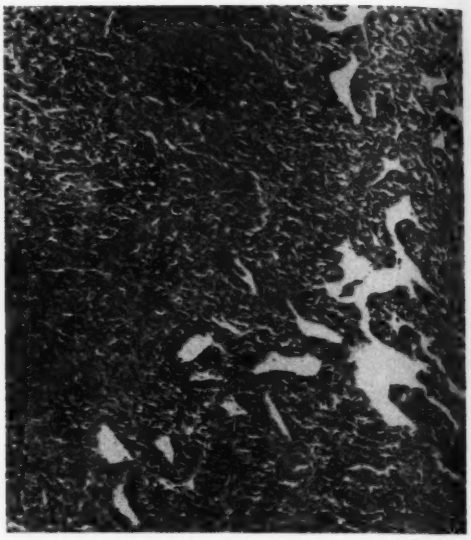
FIG. 7



Photomicrograph of first recurrence of tumor removed in 1951. Note similarity to figure 5. (H & E X 130)

slightly irregular in shape and size. Within the liver, a distinct focus of the tumor (Figs. 12 and 13) was sharply demarcated from the surrounding tumor tissue and resembled the lesion of the gingiva (Fig. 14). Both were composed of large cells with more

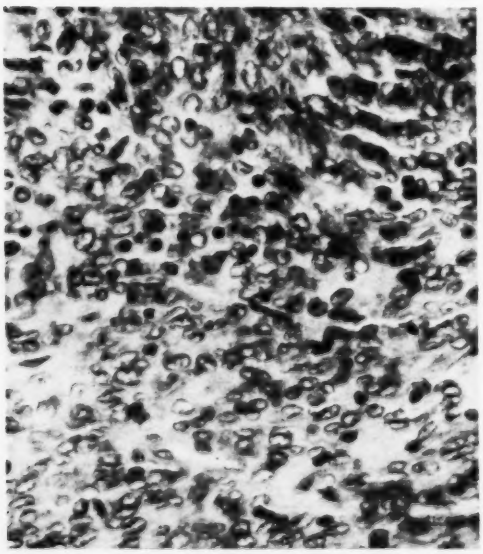
FIG. 9



Second recurrence of intracranial tumor demonstrated at autopsy. Note similarity of pattern to that shown in figures 5 and 7. (H & E X 130)

distinct coarse clumping of chromatin material, prominent nucleoli, and clear cytoplasm with indistinct cell membranes. Mitotic figures in these areas were numerous and atypical mitoses were common.

FIG. 8

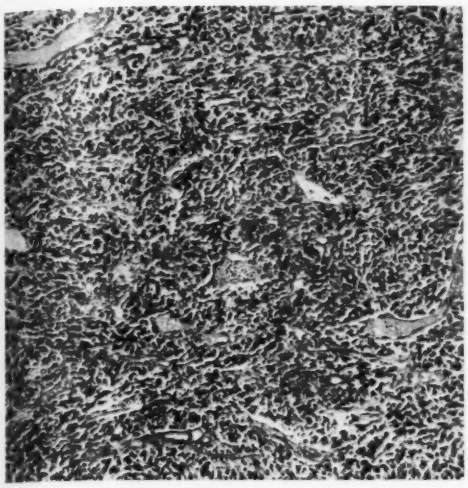


Higher magnification of the 1951 tumor illustrating the scantiness of the cytoplasm and nuclear irregularities. (H & E X 400)

FIG. 10

Compact area of autopsy specimen (1955) of intracranial lesion showing similarity of cell type as illustrated in the original lesion of 1942 (Fig. 5). (H & E X 400)

FIG. 11

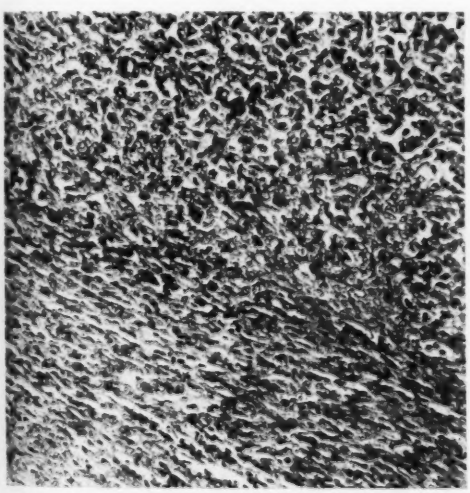


Metastatic tumor in liver showing the persistence of the whorl-like arrangement as seen in the intracranial lesions. (H & E X 130)

Discussion

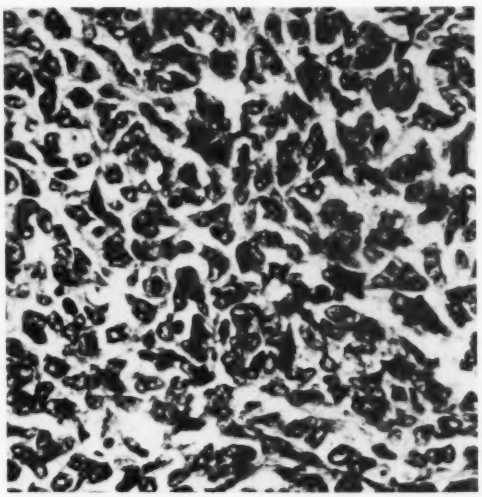
There seems to be no reliable criterion by which the occurrence of extra-cranial metastases can be predicted. Their development, considering the frequency of meningiomas in general and the rarity of those which metastasize to distant organs, appears to be largely accidental or a chance happening.

FIG. 12



Metastatic tumor in liver with sharply separated focus of histologically more malignant appearing tissue merged with the more benign appearing spindle form. (H & E X 210)

FIG. 13



Higher magnification of more pleomorphic area as illustrated in figure 12. Note mitosis. (H & E X 400)

Though perhaps more frequent in the lesions which are considered histologically malignant, the number of cases still appears too small to draw definite conclusions. This lack of gross or histologic evidence of predictability of even *local* recurrence is evident and was again graphically illustrated in a recent publication by Simpson[2] in which he cited a 9% re-

FIG. 14

Lesion from gingiva with many atypical mitotic figures. (H & E X 400)

currence rate in his Group I cases, which group was considered to be completely removed grossly, along with their dural attachment and were histologically benign.

The histologic evidence of malignancy was evident in the first sections from the specimen removed in 1942. Yet in spite of histologic signs of malignancy, the patient went 9 years before clinical evidence of recurrence became manifest with a similar tumor being removed surgically. Even at autopsy no evidence of malignancy would have been suspected from the gross appearance of the recurrent intracranial lesions. The extracranial lesions showed considerably more pleomorphism, and it would have been difficult to consider the gingival lesion as the same tumor were it not for transitional forms seen in the liver which were present to some degree in all of the intracranial lesions from 1942 and onward.

The pattern of metastases can only be accounted for by a spread by blood stream. From the slow growth of the lesion, except in the terminal phase, it is not believed possible to state whether the spread occurred from the original tumor or the second or third intracranial recurrence. This is especially true when one considers that of the 17 cases collected by Ringsted, 7 of the patients survived 13 years or longer.

Summary

A case of malignant intracranial meningioma with a local recurrence at 9 and 13 years, without gross local evidence of malignancy, is reported in which there were widespread metastases to bone, lymph nodes, liver, lungs, pancreas, kidneys and gingiva.

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2. Simpson, D.: The Recurrence of Intracranial Meningiomas After Surgical Treatment, J. Neurol., Neurosurg. & Psychiat. 20:22, 1957.

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Incidence of Ventricular and Subarachnoid Filling in Fractional Encephalography*

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and PAUL TARTELL, M.D.,† *New York City, N. Y.*

The advantages of fractional encephalography seem to be several,—relatively little discomfort, the cooperation of the patient and selective filling of certain areas as desired.

THIS IS A REPORT of 55 consecutive cases of encephalography, performed with the fractional technic of Lindgren.[1]

Our purpose was to answer:

1. Is it possible to obtain complete ventricular filling in every case?

2. Is it possible to obtain controlled filling of the cisternal and convexity spaces in every case?

3. What are the advantages or disadvantages of this method, radiographically and clinically?

Material

Fifty-five personnel on active duty and dependents seen on the neurosurgical service of the U. S. Naval Hospital, Camp Lejeune, N. C., were investigated.

The age range was 17 months to 43 years; there were 2 children. Of the adults, 33 were 17 to 21 years of age, and 20 were over 21 years of age.

The final diagnoses of the patients investigated are shown in table 1.

Technic

The patient sits erect with the head against a vertically placed x-ray table.

A lumbar puncture is done with the patient in the sitting position. A correct puncture should yield a forceful stream of cerebrospinal fluid as the stylet is withdrawn. No more fluid is allowed to escape than necessary to determine this. The position of the patient's head is then adjusted to slight flexion of the head upon the neck.

Eight cc. of air are injected very slowly, millimeter by millimeter. One minute later, lateral and posteroanterior films of the skull are taken. A Lysholm grid is used for the lateral views. The films are processed, and checked to ascertain ventricular filling. If air has reached the dorsal cerebellum without ventricular filling, the head is slightly extended and an additional 5 cc. of air are injected. Films are again made and inspected for ventricular filling. Should air appear in the ventral cisterns, the head is corrected to slightly more flexion. If further ventricular filling is deemed necessary, an additional 8 cc. of air are injected and lateral and posteroanterior films are made and reviewed. The

TABLE 1

FINAL DIAGNOSES IN 55 CASES OF ENCEPHALOGRAPHY

Epilepsy, generalized	10
Epilepsy, focal	8
Post-traumatic encephalopathy	11
Retrobulbar neuritis*	5
Multiple sclerosis (simulating tumor)	4
Postinfectious encephalopathy	3
Tumor, verified	2
Cerebral atrophy	2
Subdural hematoma, verified	1
Miscellaneous**	9

*With unusual field defects or additional symptoms.

**1 depressed fracture, 1 intracranial calcification of unknown etiology, 1 old subarachnoid hemorrhage, 1 cerebral deterioration of unknown etiology, 1 suspected cerebellar tumor, 4 psychogenic syndromes.

*Read before the Section on Neurology and Psychiatry, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

†From the Roosevelt Hospital, New York City, N. Y.

third injection of 8 cc. of air is then made with the head and neck in maximum flexion, to fill the dorsal cerebellar and collicular cisterns. Slight headache in the vertex is first noted at this stage. The two views are then repeated. If satisfactory no further air is injected. The head is then extended maximally, after which posteroanterior and lateral views are made to study the anterior cisterns (ambiens, intercrural, chiasmatic, etc.) and convexity. Should further subarachnoid filling of the convexity be necessary, the head is allowed to remain extended for several minutes. Occasionally, an additional 8 cc. of air are injected in this position.

In the average case, the total injection is 24 cc. of air. After the last injection about 15 to 20 cc. of fluid are collected. Headache and nausea may occur, but only during subarachnoid filling. Usually this is mild and the patient can cooperate with the necessary manipulations for the horizontal series.

Medication

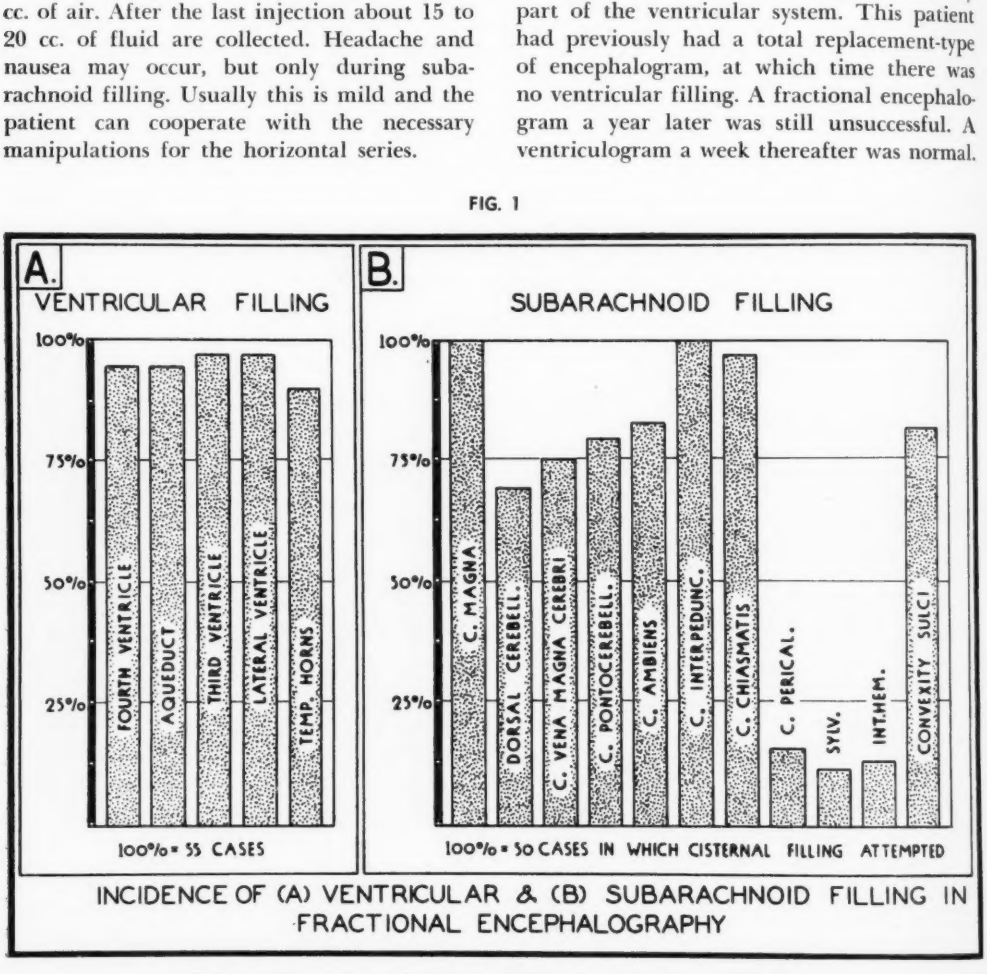
Premedication was not ordinarily given. Sedatives often made the patient dizzy. In a few cases chlorpromazine was used, but several patients fainted after sitting in the erect position for several minutes. Narcotics were unnecessary and analgesics were prescribed at the end of the procedure. Without premedication patients were routinely cooperative and comfortable. Anesthesia was used in older children.

Results

I. *Filling of the Ventricular System* (Fig. 1, A).

A. *No filling.* Of the 55 consecutive cases in our series there was one failure to fill any part of the ventricular system. This patient had previously had a total replacement-type of encephalogram, at which time there was no ventricular filling. A fractional encephalogram a year later was still unsuccessful. A ventriculogram a week thereafter was normal.

FIG. 1



Incidence of ventricular and subarachnoid filling in fractional encephalography.

It was our impression that excessive speed of the subarachnoid injection accounted for this failure. This patient had been admitted to the hospital with hematuria and severe headache. A renal tumor with cerebral metastases was suspected, but urologic and clinical study were normal.

B. Fourth ventricle. There was no visualization of the fourth ventricle in 2 patients. However, the remainder of the ventricular system except for the aqueduct of Sylvius was seen in one of these 2 cases. In this patient there was extensive cerebral and cerebellar atrophy.

C. Aqueduct of Sylvius. Of the 54 cases with ventricular filling, there was one failure to demonstrate the aqueduct, as mentioned under (B) above.

D. Third ventricle. The third ventricle was visualized in 54 cases, in lateral as well as in posteroanterior views.

E. Lateral ventricles. The lateral ventricles were visualized in 54 cases. In 10 of the 55 cases we initially filled either ventricle and found it necessary to tilt the head laterally, with the unfilled side uppermost, during the injection of an additional 5 to 10 cc. of air.

It may not be possible to transfer the air from a filled to an unfilled ventricle by simple manipulation of the head in a supine or erect position. However, further injection of air with the unfilled side uppermost, results in successful visualization with small amounts of air (Fig. 2).

F. Temporal horns. The temporal horns were visualized in 51 cases. They were seen in their entirety, including the uncinate portion with anteroposterior and lateral views. In the 3 cases in which they were seen, special views of the temporal horn had not been made.

II. *Difficulties in Filling the Ventricular System.*

A. Incorrect positioning of the needle.

No filling. An improper lumbar puncture resulted in absence of air in the intracranial spaces after the injection of 32 cc. of air in one patient. A second trial with a free flow of spinal fluid gave prompt and accurate filling.

Subdural injection. In one case, subdural injection of air resulted. No filling of the ventricular system was seen at this first attempt. At a second sitting proper positioning of the needle resulted in prompt visualization of the ventricular system and cisterns without subdural air (Fig. 3).

B. Incorrect positioning of the patient's head. In 2 patients, subarachnoid filling only was obtained after 38 cc. and 55 cc. of air were injected respectively. Maximum flexion of the head upon the neck then allowed ventricular filling to occur. In one of these 2 cases, maximum flexion of the neck was also necessary (Fig. 4).

C. Excessive speed of injection. It was noted that the single failure and the 2 cases of difficulty in filling mentioned under II, B occurred consecutively. They were the 28th, 29th and 30th cases in the series. Consideration suggested that excessive confidence in the ease of filling encountered heretofore, resulted in an accelerated speed of injection. No further difficulties were encountered after this factor was recognized and corrected in the subsequent 25 cases.

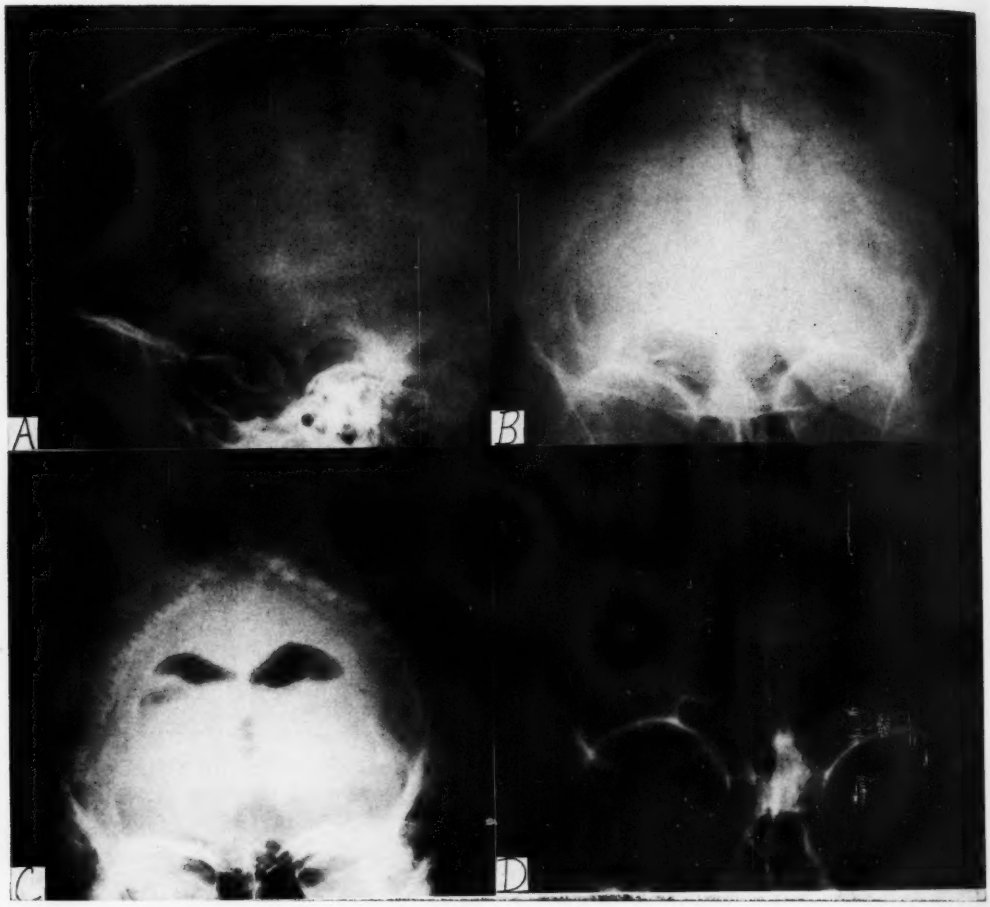
III. *Attempts to Fill the Ventricular System Primarily.*

In 5 cases, attempts to fill only the ventricular system were successful. In these cases we felt this would be sufficient to establish a

FIG. 2

Injection of 24 cc. of air. AP view with patient supine after filling of right temporal horn; moderate left ventricular atrophy.

FIG. 3



Subdural injection shown in (A) and (B). At a second sitting, 24 cc. of air in same patient is shown in (C) and (D), with no subdural air.

diagnosis (Fig. 5). In 3 cases previous arteriography studies had been obtained. In one case there was a long-standing history of petit mal epilepsy. In the last of these cases there were pronounced cerebellar symptoms in a child 8 years old. It was believed subarachnoid filling was unnecessary in view of the clinical and radiographic results obtained. When subarachnoid filling is omitted, the procedure is rewardingly painless.

IV. *Filling of the Subarachnoid Spaces* (Fig. 1, B).

Of the 55 cases in our series visualization of the cisterns was attempted in fifty. The filling of the cisterns was accomplished routinely by the injection of an additional 8 cc. of air with the head in maximum flexion. This fills the dorsal cerebellum and intercollicular cisterns and, if the patient remains in this position for 5 to 10 minutes, also the pericallosal, dorsal third ventricle cistern and the parietal sulci (Fig. 6). The air travels from the dorsal cerebellum, to the anterior cisterns by subsequent extension of the head (Fig. 7).

Of the anterior cisterns, the magna, the intercrural (interpeduncular), and the chiasmatic cisterns were filled in all cases, except for one failure to visualize the chiasmatic cistern. This was in a patient who had sustained a skull fracture with subarachnoid hemorrhage 2 weeks earlier.

FIG. 4

In (A), 45 cc. of air have been injected without ventricular filling; 53 cc. also failed to do so. In (B), maximum flexion of neck then gave good ventricular filling in the same patient with an additional 9 cc. of air.

The cisterna ambiens was clearly seen in 41 of the 50 cases.

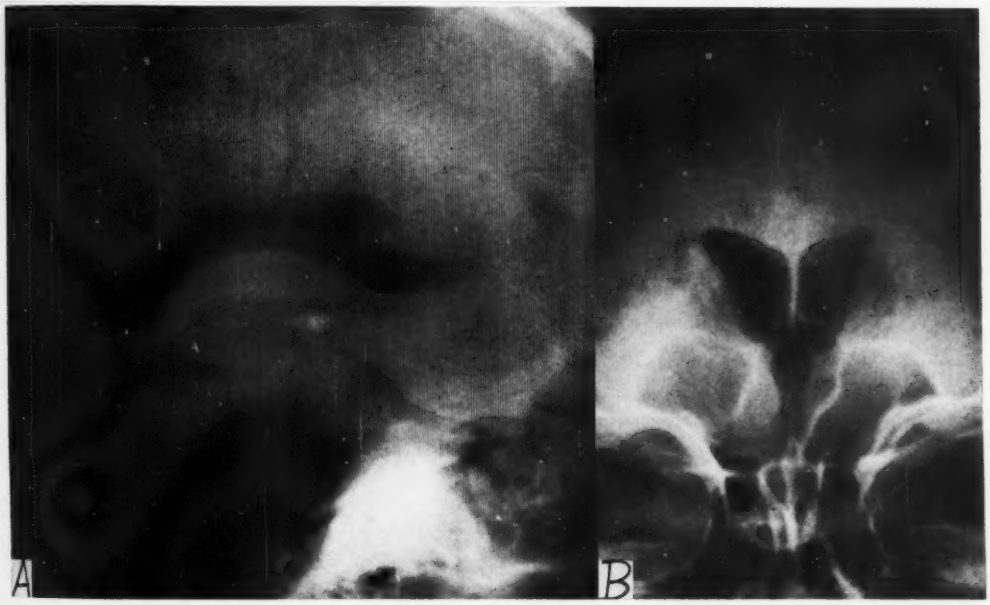
The cisterna venae magnae cerebri (intercollicular cistern) was visualized in 37 out of the 50 cases.

The pontocerebellar cistern was seen in 39 out of the 50 cases. In 17 cases the dorsal cerebellum could not be seen, but in 11 of these 17 cases, the pontocerebellar cistern was visualized.

More diligent positioning of the patients resulted in filling the dorsal cerebellar cistern in the last 17 consecutive cases.

Similar experience was encountered with

FIG. 5



Sixteen cc. of air gave the excellent ventricular filling shown in (A) and 22 cc. in (B), where subarachnoid filling was not required.

FIG. 6

Erect (A) lateral and (B) PA views with 28 cc. of air, to show in (A) dorsal cerebellar, collicular and pericallosal cisterns and parietal sulci, and in (B) collicular, ambiens, pontocerebellar cisterns.

the pontocerebellar cisterns, with 16 out of the last 17 cases resulting in satisfactory visualization.

The convexity. Subarachnoid air was seen over the cerebral hemisphere in 41 out of 50 cases in which attempts were made to fill the cisterns routinely. In 40 cases no additional air was required. The air which was in the basilar cisterns was sufficient in amount to give adequate visualization of the convexity if the head was left in extension for 5 to 10 minutes. On one occasion an additional 10 cc. of air was injected with the head in extension, in an attempt to further localize a subdural hematoma. The air filled the left frontal pole and medial frontal area. Operation revealed a lateral frontal-temporal subdural hematoma.

The Sylvian, pericallosal and interhemispheral cisterns did not fill routinely with this amount of air, or with the positioning of the head that was routinely used. The pericallosal cistern was visualized in 12 of the 50 cases, interhemispheral air was seen in 11 of 50 cases, and the Sylvian subarachnoid air was seen in 8 of the 50 cases.

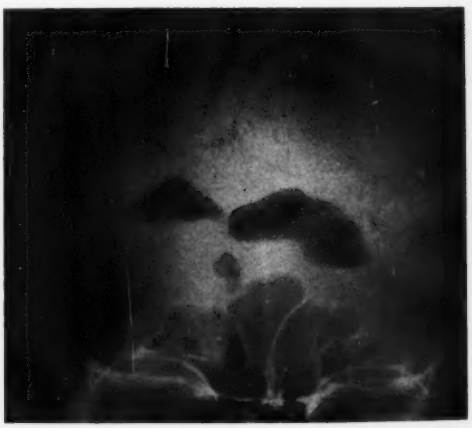
V. *Space Occupying Lesions.*

This series includes three verified space occupying lesions: one subdural hematoma in the left frontal temporal region (Fig. 8), one

FIG. 7

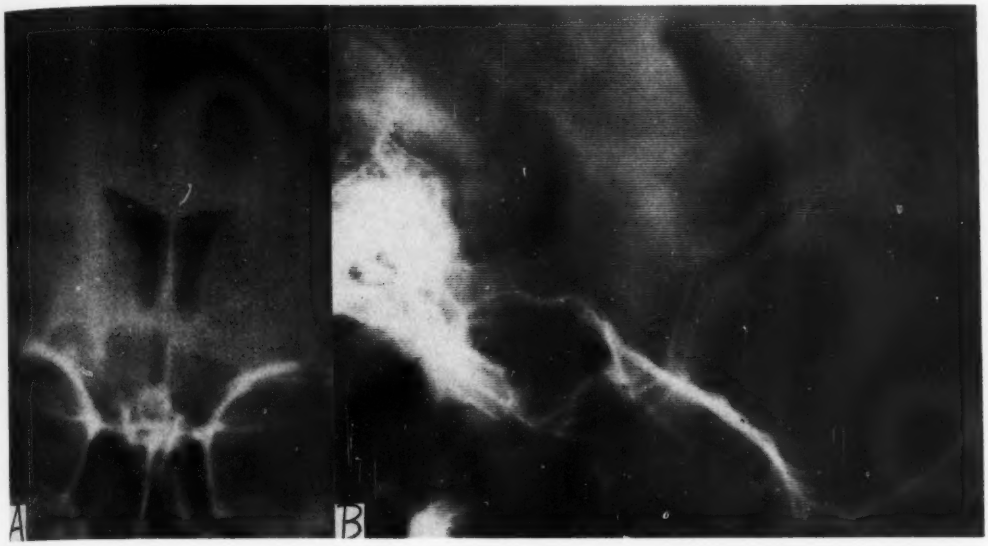
Extension of the head produces filling of the anterior cisterns; pontis, interpeduncularis, chiasmatic, shown here.

FIG. 8



PA erect, 25 cc. of air injected. A shift of the ventricular system toward the right verified a left frontal-temporal subdural hematoma.

FIG. 9



Ten cc. of air were injected in a 9 year old patient with cerebellar symptoms. AP (A) and brow-up (B) views.

right temporal fibrillary astrocytoma, and one central convexity fibrillary astrocytoma. In these 3 cases, encephalography gave accurate localization with good ventricular and cisternal filling.

Encephalography was not done in suspected tumor of the posterior fossa with clinical evidence of increased intracranial pressure.

VI. *Encephalography in Children.*

In this series one infant 17 months old was investigated under local anesthesia. The clinical diagnosis was cerebellar atrophy. This was confirmed by encephalography which revealed cerebral and cerebellar atrophy. A total of 30 cc. of air were used in this patient with filling of the ventricular and subarachnoid spaces, except for the fourth ventricle and aqueduct. In one 9 year old child, suspected of having a cerebellar tumor, 10 cc. of air gave excellent visualization of the fourth ventricle, aqueduct, and third and lateral ventricles (Fig. 9). This was the only patient in our series in whom general anesthesia was used.

Summary

1. Fifty-five consecutive cases of fractional encephalography are reported with the incidence of ventricular and subarachnoid filling.

2. Adequate ventricular filling was obtained in 54 cases.

3. Controlled and selective filling of the basilar cisterns and convexity was possible in most cases. There was filling of the anterior cisterns in 98%; of the cisterna ambiens in 82%; filling of the cerebellar cisterns in 88%; and showed filling of the convex spaces in 82 per cent.

4. The disadvantages of the procedure are the time consumed in performing the examination, the constant attention of the neurosurgeon and radiologist to modify technics, and the large number of films used.

The advantages are the excellent visualization of the posterior fossa, the selective filling of the areas desired, the relative comfort under local anesthesia, the cooperation of the patient for changes of position, and decreased headache after procedure.

5. As experience with the technic increased the results obtained improved.

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Periarticular Ossification Following Burns*

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Gastonia, N. C.

It seems likely that some metabolic disturbance underlies the periarticular ossification which may occur in association with extensive burns of the skin.

PERIARTICULAR OSSIFICATION following burns was first described in the English literature by Johnson in 1957.[1] In his paper he reported three patients who developed this complication following severe burns. Periarticular ossification or myositis ossificans has been reported in most all parts of the body, and in most patients it has been related to trauma as reported by Shipley.[2] It was his belief that with trauma the periosteum is stripped off with resultant hemorrhage and calcification. Shipley also felt that the systemic condition of the patient was not a significant factor in the production of myositis ossificans, and found all blood values to be normal. It was his belief that the local reaction of tissue is the important thing, but was unable to describe what conditions were necessary to produce this metaplasia in some patients and not in others. The most common factor in all of his cases was closed trauma.

Costello and Brown,[3] in 1951, reported three cases of myositis ossificans in poliomyelitic patients. They mentioned that Degerine, in 1919, had found myositis ossificans in patients with traumatic paraplegia. Hess[4] and Frieberg[5] also noted myositis ossificans in patients with poliomyelitis. Heinen and his associates,[6] working with rabbits, came to the conclusion that the intramuscular injections of extracts of bone or cartilage do not produce myositis ossificans more frequently or more extensively than the extracting fluid alone, and postulated that there is no osteogenic substance necessary for its production.

Johnson[1] tried to rule out any major or chronic trauma as being the etiologic agent in the production of atypical myositis ossificans, but pointed out that in most all of his patients there had been multiple changes of dressings under general anesthesia and the possibility of trauma could not be completely ruled out. He found the common features in all of his cases were relative immobility of the patient, a precarious general condition with altered protein, electrolyte, and fluid balance, and decreased vitality of local tissues with edema and poor circulatory flow.

At the North Carolina Orthopaedic Hospital, in Gastonia, N. C., where approximately 1,000 burn cases have been cared for in the past 25 years under the supervision of Dr. William Roberts, a review of these records has yielded 6 children who developed periarticular ossification as a complication of their burns. Most of these children received their initial treatment in some general hospital and were transferred to the Orthopaedic Hospital at about an average of 2 weeks after the initial burn. The following are summaries of these 6 patients.

Case Reports

Case 1. D. C. (No. A-2325), a 5 year old girl was burned about the abdomen, buttocks, and legs when her clothing caught fire in Apr., 1947. She had initial treatment elsewhere, including all skin-grafting, and was admitted to the Orthopaedic Hospital for excision of a dense scar over the perineum and regrafting of these areas. While there she developed a flexion contracture of the right hip. She was discharged in July, 1948, walking fairly well.

She returned in July, 1949, with complete ankylosis of the right hip which was in good position. X-ray examination at that time revealed periarticular ossification extending from the inferior aspect of the neck

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

†From the Miller Clinic, Charlotte, N. C., and the North Carolina Orthopaedic Hospital, Gastonia, N. C.

FIG. 1

Periarticular ossification extending from the femoral neck to the ischium. Note partial subluxation of the femoral head, right hip.

of the femur to the ischium of the pelvis (Fig. 1).

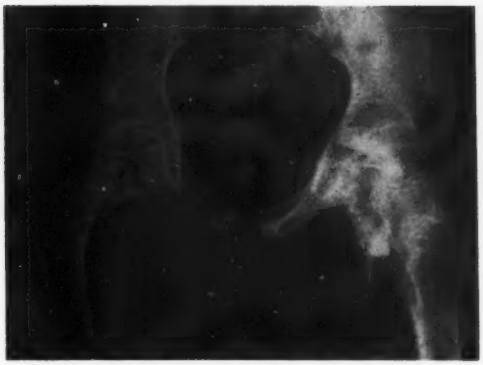
Since this child walked well with the stiff hip no reconstructive procedure was done. She was last seen in 1953 at which time she had no complaints in spite of the ankylosed hip.

Case 2. A. H. (No. A-472), a 13 year old girl received third degree burns about the stomach, chest, neck, right thigh, and arms in Aug., 1943. The skin overlying the left hip was not burned, nor was the skin over the left elbow involved. She received her first 2 weeks of care elsewhere.

She was admitted to the Orthopaedic Hospital in Gastonia for split thickness grafts to the burned areas. Considerable limitation of motion developed in both hips and in the left elbow while under active treatment. X-ray films revealed periarticular ossification about both hips (Fig. 2, A) and the left elbow anteriorly (Fig. 2, B). No attempt was made to excise these ossified areas.

Case 3. D. P. (No. A-7039), a 3 year old girl received third degree burns about the abdomen, perineum, buttocks, and legs down to the knees, in Oct., 1954, when her clothing caught fire. Skin-grafting was done at the North Carolina Orthopaedic Hospital, and she developed considerable limitation of motion in both hips. The hips were manipulated on one occasion in the hope of increasing the hip joint motion, but without success. Following manipulation x-ray films showed marked periarticular ossification about both hips (Fig. 3).

FIG. 3



Marked periarticular ossification about both hips, worse on the right. Note partial subluxation of the right hip.

This child walks with a bilateral stiff hip gait, but no attempt has been made to excise the periarticular ossification.

Case 4. T. L. (No. A-5891), was a 5 year old girl who received burns to the trunk, thighs, and left arm down to, but not including the skin over the elbow joint, after her clothing caught fire. She developed ankylosis of the left elbow one month after the burn, and x-ray studies revealed a large amount of periarticular ossification about the elbow (Fig. 4).

The child died of complications several months after

FIG. 2

A B

(A) Periarticular ossification about both hips, more marked on the left. (B) Periarticular ossification anterior left elbow joint with the joint fixed at 90 degrees.

FIG. 4

Periarticular ossification about the left elbow completely bridged anteriorly but incomplete posteriorly.

the burn. No reconstructive surgery of the elbow was done to give any increased motion before death.

Case 5. A. M. (No. A-7047), a 6 year old girl received third degree burns about both thighs, the stomach, and perineum in Oct., 1954, when her clothing caught fire. She had split thickness skin-grafting to the burned areas at the North Carolina Orthopaedic Hospital. While under active treatment, approximately 6 months after the initial burn, she developed a fixed contracture of the right hip, and an x-ray examination revealed a large area of periarticular ossification about this hip (Fig. 5).

FIG. 5

Periarticular ossification about the right hip. Note joint space and femoral head obliterated by new bone formation.

FIG. 6

Periarticular ossification with complete bridge posterior humerus and tip of olecranon.

The child, in spite of this contracture, was able to get around quite nicely and no operation was done on this hip.

Case 6. B. B. (No. A-7728), a 10 year old girl received burns about her trunk, thighs, and arms when her clothing caught fire. She received all of her split thickness skin-grafts at the North Carolina Orthopaedic Hospital; no manipulations were carried out about the elbow. She developed an area of periarticular ossification about the right elbow with marked limitation of motion. This mass of new bone was excised as completely as possible on one occasion, and a slight increase in the motion of the elbow was obtained. About 2 months later this motion was lost, and an x-ray film revealed recurrence of the ossification (Fig. 6).

Comment

These 6 patients represent an incidence of less than one per cent of all burned patients treated at the North Carolina Orthopaedic Hospital. Why these children with third degree burns should develop periarticular ossification and the many others treated not develop it is difficult to state.

It is of particular interest to note that in 2 of these patients the calcification occurred about joints whose covering skin was not directly involved in the burned process. Also, in none of the cases presented here was it felt that the burn extended down to the capsular structures about any of the joints. These two

factors certainly are suggestive that some alteration in the metabolism plays a large role in the production of the periarticular ossification but, as Johnson and others have pointed out, no specific chemical alterations in the blood values have been found. Another interesting observation in these 6 patients is that all were girls, and although Johnson did not point this out in his report, his 3 cases were in females. Because of the universally poor results in excising myositis ossificans secondary to trauma, only one child in this series has been submitted to operation, and in this one there was an immediate recurrence of the ossification at the operative site. The production of myositis ossificans and periarticular ossification falls into the realm of bone physiology that still is not well understood.

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A New Method for Identifying Blood of the Portal Circulation*

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The authors recount their findings by a new experimental approach in an attempt to evolve a method for determining the origin of blood in bleeding in portal cirrhosis.

Purpose

THE STUDIES described in this paper were carried out with the long range objective of attempting to develop a method for differentiating bleeding esophageal or gastric varices from hemorrhage in the upper gastrointestinal tract due to other causes. The achievement of this objective is dependent upon the validity of the following concepts: (1) an identifiable material can be introduced into the portal circulation of a patient with hemorrhage in the upper gastrointestinal tract; (2) a concentration of this identifiable material can be obtained in the blood of the portal circulation that is sufficiently higher than in the blood of the systemic circulation to permit differentiation of the two; (3) blood in the portal circulation is shunted into the systemic circulation through esophageal or gastric varices in patients with portal hypertension, and if a varix ruptures blood of the portal circulation enters the stomach; and (4) if the blood of the portal circulation contains an identifiable material in significantly higher concentration than does blood in the systemic circulation, blood aspirated from the stomach of a patient with a ruptured varix can be identified as escaping from the portal circulation.

To date we have investigated only the first two of the above concepts, and this report deals with the methods employed in and the results of experiments pursued in the development of technics for differentiating blood in the portal circulation from blood in the systemic circulation. This investigation has been carried out in dogs except for one group of human experiments.

Procedures

Possible approaches to the portal circulation were considered, bearing in mind that any technic developed should be applicable to a patient suffering from massive loss of blood. We elected to explore the possibility of introducing materials into the portal circulation by means of absorption through the wall of the bowel within reach of a sigmoidoscope.

Initial experiments involved the injection of a dye into the wall of the sigmoid colon of dogs from the serosal surface through an abdominal incision. Blood specimens obtained from the portal vein and the vena cava then were compared in regard to dye concentration. Following injection of a 2% solution of sodium fluorescein with hyaluronidase added, dye appeared promptly in the blood of the portal vein in a concentration sufficiently greater than that found in vena caval blood so the two could be distinguished one from the other. The next step was to devise a safe technic for injecting the dye into the bowel wall from inside the lumen. The simple method of inserting a long needle through a sigmoidoscope and piercing the bowel at the end of the instrument proved unsatisfactory as did various devices for carrying a small syringe through the sigmoidoscope. Frequently, either the needle did not enter the bowel wall at all or it went completely through into the peritoneal cavity.

An instrument finally was devised by means of which the bowel wall can be injected with

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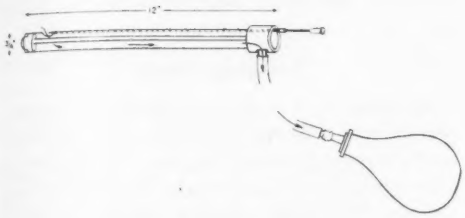
FIG. 1



relative ease. This is depicted in figure 1 and is a length of stainless steel tubing made into a sigmoidoscope with certain modifications. These consist of a hole in its wall near the distal end, a channel in the wall leading from the proximal end to the edge of this hole, and an airtight viewing cap which slips over the proximal end. This cap has a channel in its wall which is continuous with that in the wall of the sigmoidoscope. It is also fitted with a side tube through which suction can be applied. Upon applying suction, mucosa herniates through the distal hole. A long needle then is inserted through the channel in the wall of the instrument and plunged into the herniated mucosa.

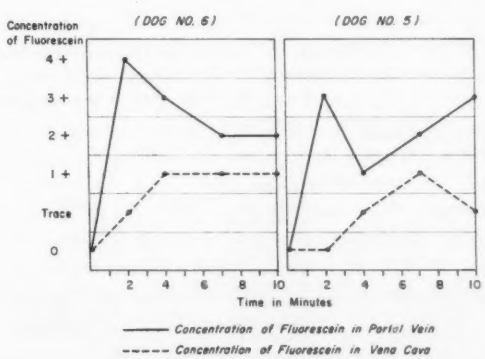
Six dogs were handled experimentally in the following manner. Anesthesia was obtained by the intravenous injection of a solution of pentobarbital sodium, and an abdominal incision was made to expose the portal vein and the vena cava. After securing preliminary blood specimens from each vessel and removing all feces from the lower bowel through a standard sigmoidoscope, 1.0 ml. of a 2% solution of fluorescein together with 150 units of hyaluronidase was injected into the bowel wall by means of the modified sigmoidoscope. Specimens of blood were taken from the portal vein and from the vena cava at 2, 4, 7 and 10 minutes following injection of the dye. Each of these blood specimens was examined for its content of fluorescein as described below.

A protein free blood filtrate was prepared by making a slight change in Haden's modification of the method of Folin and Wu. As routinely carried out, this procedure results in precipitation of fluorescein as well as protein. However, we found that the addition of 10 ml. of a 70% solution of isopropyl alcohol causes fluorescein to go back into solution without disturbing the precipitated protein material. The filtrate obtained is a 1:20 dilution of the original blood sample, and has an acid reaction in which fluorescein does not exhibit fluorescence. However, upon adding a small amount of strong alkali to the filtrate the fluorescent property for fluorescein returns. We arbitrarily took 7 ml. of each filtrate and added 0.5 ml. of a 50% sodium hydroxide solution to each in order to obtain uniform specimens for examination in regard to fluorescence. All specimens from a single dog experiment were examined at one sitting under ultraviolet light and judged by the examiner to exhibit fluorescence in degrees of zero, trace, and one to four plus. At the time of estimation, the examiner did not know the source or time interval of any specimen.

Results

In all dogs fluorescein could be found in blood from the portal circulation 2 minutes after injection of the dye into the bowel wall. The concentration of dye in blood from the portal vein was consistently higher than that in blood taken from the vena cava. Figure 2, A, illustrates the most satisfactory experiment. In this animal, the maximum concentration of dye in the portal circulation had been achieved by 2 minutes and it fell off thereafter. At the same time, the concentration of dye in the vena cava increased more gradually, and its maximum is considerably less than the maximum concentration of dye in the portal circulation. Figure 2, B, illustrates our least satisfactory experiment. In this animal, the concentration of dye in both portal and systemic circulations appears erratic and suggests that, although absorption

FIG. 2



of dye from the bowel wall was prompt, it was irregular. However, even in this animal the maximum dye concentration obtained in blood from the portal vein was significantly higher than the highest concentration found in blood from the vena cava.

Our projected concept regarding the possible application of this technic to identification of hemorrhage from the portal circulation involves constant aspiration of blood from the stomach, and separating this blood into fractions. Each fraction would be the volume of material aspirated during a selected period of time, for instance one minute. If the concentration of dye in any fraction is greater than the concentration of dye in the systemic circulation (blood from an antecubital vein), we believe this would indicate bleeding from the portal circulation. If this concept is valid, the most significant determination in these experiments is the difference between the highest concentration of dye found in the portal circulation and the highest found in the systemic circulation. Table 1 permits comparison of the maximum concentrations of dye obtained in each circulation during all experiments. Using the five point scale already described for evaluating the degree of fluorescence of specimens, the difference in maximum dye concentration between the two circulations was two points in three experiments, three points in two experiments, and four points in one experiment. In all instances one had no difficulty in perceiving that the brightest of the specimens from the vena cava exhibited less fluorescence than did the brightest of the specimens obtained from the portal vein. In three of the six experiments no specimen from the vena cava exhibited as much fluorescence as did the least concentrated specimen obtained from the portal vein.

Pathologic Study

Six dogs were studied to determine whether injection of sodium fluorescein into the bowel wall causes significant damage. Each dog was anesthetized with a solution of pentobarbital sodium following which a small abdominal incision was made under sterile conditions. The area of the sigmoid colon to be injected was exposed. Injection of the dye was carried out as previously described except that the modified sigmoidoscope and needle were sterilized. As soon as the injection had been completed, the injection site was marked by placing two silk sutures in the serosa on either side of it. The abdomen then was closed immediately without securing any blood specimens.

Half of these dogs were sacrificed 3 days and the other half 4 days after injection. The bowel segment containing the injection site was submitted for pathologic examination. Microscopic study revealed peritoneal reaction in all specimens, but this appeared to have been caused by the marking sutures rather than being the result of the injection. The opinion of the pathologist (W.A.D.A.) was that the injection itself did not cause significant damage to the bowel wall.

Further Procedure

The ease with which trace amounts of radioactive materials can be identified when suitable equipment is available led us to pursue the possibility of employing such a substance in the same manner as we had used

TABLE 1

MAXIMUM CONCENTRATIONS OF FLUORESCEIN IN PORTAL VEIN AND IN VENA CAVA

(The time at which these maximum concentrations occurred is indicated.)

Experiment Number	*Source of Blood*	*2 Min.*	*4 Min.*	*7 Min.*	*10 Min.*
1	Portal vein		4+		
	Vena cava				2+
2	Portal vein			4+	
	Vena cava	Trace			
3	Portal vein		3+		
	Vena cava				1+
4	Portal vein		3+		
	Vena cava	Trace			
5	Portal vein	3+			
	Vena cava			1+	
6	Portal vein	4+			
	Vena cava		1+		

fluorescein. Because of its ready availability to us, we selected iodine-131. As will be commented upon later, this selection probably was unwise, but results obtained with this material may have application to other materials.

Preliminary experiments in dogs revealed that radioactive iodine appears promptly in the portal circulation following injection into the bowel wall, but administration by this technic appeared to have no advantage over simple instillation into the lumen of the bowel.

Using the simpler instillation technic the rate of mucosal absorption of I^{131} was investigated in humans by introducing 10 to 25μc. of I^{131} in a volume of 0.5 ml. into the lumen of the bowel by means of a long needle passed through an inserted sigmoidoscope. Blood specimens were taken from an antecubital vein at 2, 5, and 10 minutes after administration of the I^{131}. The radioactivity of these specimens was determined by placing 5.0 ml. of whole blood in a scintillation well counter and making counts in the usual manner.

Our interest centered upon achieving speed in absorption of the total amount of I^{131} administered. The end point of complete absorption is a constant or decreasing level of radioactivity in the systemic circulation. As complete absorption approaches, the level of radioactivity in the systemic circulation increases at a progressively slower rate or, in other words, the absorption curve flattens. As a means of comparing the mucosal absorption rates of different individuals we have used the flattened end of the absorption curve and expressed this in terms of the per cent increase in radioactivity occurring between 5 and 10 minutes. The smaller this per cent increase is, the more rapid and complete has been absorption during the early part of the experiment.

TABLE 2

PATIENTS RECEIVING I^{131} IN PHYSIOLOGIC SALINE

Patient	Radioactivity Counts Per Minute 2 Min.	5 Min.	10 Min.	Per Cent Increase 5-10 Min.
1	326	1440	2357	64%
2	168	1878	3224	72%
3	60	871	1431	64%
4	75	400	732	83%
5	119	451	903	100%
6	142	786	1353	72%
Average	148	971	1667	76%

TABLE 3

PATIENTS RECEIVING I^{131} IN ALCOHOLIC SOLUTION

Patient	Radioactivity Counts Per Minute 2 Min.	5 Min.	10 Min.	Per Cent Increase 5-10 Min.
1	412	517	766	48%
2	956	1289	1267	0
3	536	556	801	44%
4	209	224	210	0
5	31	489	543	11%
6	500	815	905	11%
7	297	752	818	9%
8	1027	2445	2275	0
9	1016	2235	2268	1%
Average	554	1036	1095	14%

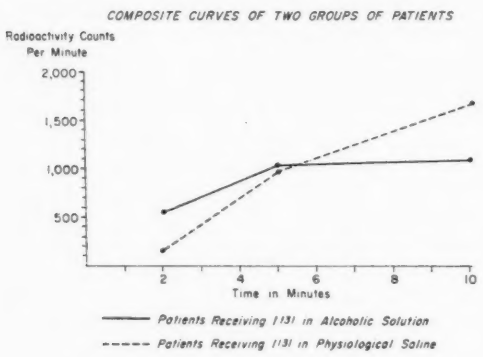
Results

Data obtained from 6 patients receiving I^{131} in 0.5 ml. of physiologic saline are presented in table 2. The lowest per cent increase in radioactivity between 5 and 10 minutes was 64%, and the average for all 6 patients was 76%, indicating that in this group of patients considerable absorption of I^{131} continued after 5 minutes.

Data obtained from 9 other patients receiving I^{131} in 0.5 ml. of a 50% solution of ethyl alcohol are presented in table 3. The per cent increase in radioactivity between 5 and 10 minutes was much less in this group of patients than in those receiving I^{131} in saline. In 3 of these patients no increase in radioactivity occurred after 5 minutes, and in only 2 was it over 12 per cent. The greatest increase was 48%, and the average of all 9 patients was 14 per cent.

Figure 3 presents composite curves of the two groups of patients. These were prepared by taking the average of the actual counts per minute at each time interval. In evaluating these curves one should bear in mind that the amount of I^{131} administered to each patient was not constant. However, it is apparent that, while the 10 minute counts averaged higher in those patients receiving I^{131} in saline, the 2 and 5 minute counts were higher in those patients in whom an alcoholic solution was used. Furthermore, in the latter group the curve between 5 and 10 minutes is nearly flat.

FIG. 3



Comment

The introduction of identifiable materials into the portal circulation by way of the lower bowel within reach of the sigmoidoscope is possible, and a sufficiently high concentration can be obtained to differentiate between blood from the portal vein and blood from the vena cava. This has clinical significance only if further investigation reveals that blood aspirated from the stomach of an individual bleeding from a ruptured varix can be identified as coming from the portal circulation following the procedure.

The procedure of injecting fluorescein into the bowel wall appears ready for human trial. On the other hand, the instillation of an absorbable material into the bowel lumen is a simpler procedure, and the identification of a radioisotope can be accomplished with great ease and rapidity when suitable equipment is available. The latter procedure appears to us to be the preferable one. Iodine-131 has been useful in our attempt to develop technics, particularly in the demonstration that the mucosal absorption rate can be influenced markedly by the vehicle containing the tracer material. However, the use of I^{131} to identify blood aspirated from the stomach is complicated by the fact that iodide appears in gastric juice in a concentration much higher than that found in the peripheral blood. This was reported, in 1894, by Nencki and Schoumow-Simanowsky.[1] Davenport[2] and Mason and Bloch[3] have studied this phenomenon in dogs, and Schiff[4] and his co-workers reported it in humans. We have made assays for radioactivity on gastric specimens obtained from some of our patients, and the results have been in agreement with these investigators. This property of iodide probably precludes the practical use of I^{131} in bleeding patients. We hope that another radioisotope can be found to have the absorption properties of I^{131} without the complication noted.

Summary

1. A concept for detecting the escape of blood from esophageal or gastric varices by introducing an identifiable material into the portal circulation and then finding a significant concentration of it in blood aspirated from the stomach has been presented.

2. Identifiable materials were introduced into the portal circulation of dogs by injection into the wall of the lower colon by means of a modified sigmoidoscope. The injection of fluorescein resulted in portal vein concentrations of dye consistently higher than concentrations in the vena cava. Pathologic study revealed no significant damage to the bowel of dogs in which this technic was used.

3. Radioactive iodine instilled into the lumen of the lower bowel was found to be absorbed just as effectively as that injected into the bowel wall. Human experiments demonstrated an increased absorption rate when it was instilled in an alcoholic solution as compared to instillation in physiologic saline.

4. Further investigation is required to determine whether or not these observations can be applied to the practical problem of identifying hemorrhage from a ruptured esophageal or gastric varix. The secretion of a high concentration of iodide by the gastric mucosa, as found by other investigators, probably precludes the use of iodine-131 for this purpose.

Acknowledgments

We owe an expression of appreciation to: Shirley Litz, R.N., whose efforts contributed a great deal to the conduct of this investigation; Robert Litwak, M.D., who made it possible for us to use dogs which later were used in his investigative work; Becton, Dickinson and Company for supplying us with tubing and long needles required in the development of apparatus for making injections in the bowel wall; and the Wyeth Laboratories for supplying us with the hyaluronidase (Wydase) used in this study.

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Discussion (Abstract)

Dr. Spalding Schroder, Atlanta, Ga. As we all know, duodenal ulcer is more common among patients with cirrhosis than among those without, and once bleeding starts hemostatic deficiencies secondary to the liver disease seem to be important in prolonging it. Also, the patient with cirrhosis is particularly susceptible to acute erosive gastritis which may result in massive bleeding. Portal hypertension is undoubtedly responsible for both occurrences just as it is responsible for the development of esophagogastric varices.

As Dr. Shorey's technic is developed further, it will be of greatest interest to investigate the concentration of the test material in the tributaries of the gastric veins and their capillaries, under various circumstances. One might speculate that the results would differ, depending on the venous pressure within these vessels. In the normal the concentration would be expected to equal that of systemic veins. In the presence of advanced portal hypertension without hemorrhage, there might be a higher concentration of test material in these veins than in systemic veins, due to the marked pressure increases manifested by engorgement of the submucosal veins of the stomach and duodenum so characteristic of cirrhosis. Finally, in advanced portal hypertension with venous bleeding due to acute erosive gastritis or peptic ulcer, one might speculate that the test material might follow the path of least resistance and appear in the gastric lumen in significant quantities, just as would be expected in bleeding from esophagogastric varices. If such armchair speculation proved correct, the clinician would be hard-put to identify the source of bleeding since in all three circumstances the material would be escaping from the portal circulation.

Fifty-third Annual Meeting of Southern Medical Association in Atlanta, Ga., November 16-19, 1959

Blood Flow Determined by the Use of Radioiodinated Serum Albumin and an Externally Placed Scintillator Detector*

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The authors offer a new tool which may make determinations of blood flow in certain areas of the body more feasible and much simpler than by methods now in use. This has great diagnostic and prognostic implications.

Introduction

SIMPLY PERFORMED TECHNICS for qualitative estimation of peripheral blood flow have been described.[1-4] However, convenient methods for quantitative estimation of blood flow through peripheral organs have not been available. Up to the present time, all published methods for the quanitative estimation of blood flow have required the inconvenience of intravenous or intra-arterial catheterization. The only exception to this is the kidney where the clearance of Diodrast or sodium para-amino hippurate can be used to estimate renal blood flow.

While the Diodrast and sodium para-amino hippurate clearance technics for the measurement of kidney blood flow have been used extensively, these methods have two limitations. First they require nearly normal tubular function and, secondly, it is necessary to do ureteral catheterization for estimation of individual kidney blood flow.

In 1949, Prinzmetal and associates[5] described a method for determination of cardiac output, using radioactive sodium as a tracer and avoiding arterial blood sampling by placing a Geiger-Mueller tube over the precordium. The cardiac output values as subsequently developed compared favorably with those obtainable by other methods and this work has since been confirmed by several investigators.[6-8]

We wish to report a method of using an externally placed radiation detector for the quantitative measurement of blood flow through not only the heart but also in peripheral organs, particularly each kidney, uterus and coronaries. This method is simple, nontraumatic and lends itself to clinical diagnosis.

Materials and Methods

Twenty microcuries of radioiodinated human albumin are injected into the antecubital vein to supply the circulating tracer. Proper precautions must be observed to prevent a holdup of the bolus in the arm.[5] The equipment consists of a well-shielded scintillation detector with a collimeter head 1 inch in diameter and 2 inches deep, a ratemeter with a very short time delay (0.5 seconds to go full scale of 10,000 counts per minute) and a milliamperere recorder, recording at a speed of 12 inches per minute. Such an assembly constitutes one individual channel. One such channel is used always with its detector located over the heart region to measure cardiac output and coronary blood flow. The detector is placed on the skin medial to the projection of the left pulmonary artery on the anterior chest wall. This point is determined by using a chest x-ray film. Another detector is located over the peripheral organ whose blood flow

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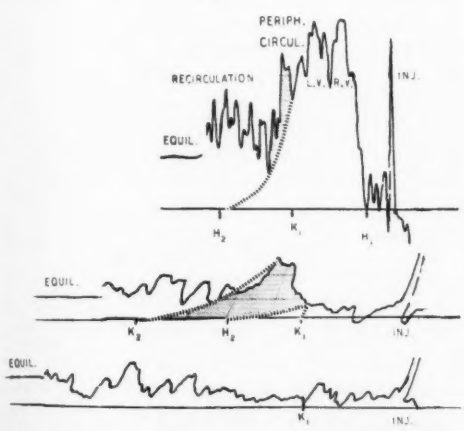
is to be determined. In determining kidney blood flow we have used two such peripheral channels, one for each kidney. The surface projection of the kidney is determined by using a plain x-ray film of the abdomen.

Cardiac output is determined by the method of Prinzmetal and associates,[5] and the ratio between cardiac output and the organ blood flow during the first circulation of the radioactive tracer is determined simultaneously. By dividing the cardiac output by this ratio we obtain an estimate of the blood flow in the peripheral organ.

In figure 1 are shown three tracings obtained simultaneously. The top tracing is recorded with the detector placed in the heart area and the lower two with the detector in the left and right flank areas on a patient with aplasia of the right kidney. The single sharp peak to the extreme right represents the time of injection on each curve. After a short delay, while the injected tracer dose passes from the injection point to the heart, there appears on the heart curve two high peaks representing the passage of the tracer dose through the right and left heart circulation.

In the tracings from the detectors placed over the kidney area these two heart peaks are poorly defined because of the distance from the heart and because the detectors are collimated. At the time the tracer dose passes from the left ventricle into the peripheral circulation there appears on the middle tracing a well-defined peak representing peripheral circulation in this kidney area. No such peak appears on the tracing recorded from the right flank area where no kidney was present. On the heart tracing a similar peak from the peripheral circulation appears at the same time as the kidney peak. The peaks from the peripheral circulation appear at the same time in each area because the speed of the blood passing through the aorta is so much faster than our recording speed.

FIG. 1



Time activity curve recording the passage of radioiodinated serum albumin through the heart and left kidney. This patient had a congenital aplasia of the right kidney. A rectilinear recorder was used only for the heart tracing. Top tracing is over the heart, middle tracing over left flank and bottom tracing over right flank.

Each peak is extrapolated to the base line using the curve of best fit obtained from a logarithmic spiral or a French curve. The time between the beginning of each peak and the extrapolated point at which it reaches the base line is the transit time of the radioactivity through each organ.

The area beneath each peak is determined with a planimeter realizing that none of these peaks overlap. The equilibrium radioactivity of each channel is determined after complete mixing of the tracer has occurred (10 minutes approximately).

Cardiac output and organ blood flow are estimated using the following formulas. Their derivation will be published elsewhere.

$$F_h = \frac{I_h}{A_h \cdot f \cdot C_h}$$

$$\frac{I_h}{I_p} = \frac{A^2_h \cdot T_p \cdot E^2_p}{A^2_p \cdot T_h \cdot E^2_h} = \text{ratio}$$

$$F_p = \frac{F_h}{\text{ratio}}$$

Subscript h = heart, p = peripheral organ (kidney or coronary), I = amount of radioactive tracer, A = area under the peaks, T = transit time, E = efficiency factor, cpm of a standard dose from each detector, C = ratio between cpm/ml blood and cpm on recording at equilibrium, f = transforms sq cm on curve to cpm/secs. The E for heart and coronary cancel out.

Para-amino hippurate clearances were performed by a standard method.[9]

Results

In table 1 are presented the normal range of values of cardiac output obtained by this method in 50 patients without clinically evident cardiovascular disease. The mean age plus or minus the standard error of the mean of these patients was 43 ± 2 years and their mean weight was 157 ± 3 pounds. The total

TABLE 1

CARDIAC OUTPUT IN 50 PATIENTS WITHOUT KNOWN CARDIOVASCULAR DISEASE

	Normal Range	*Mean ± S.E.*
Liters/min.	6.8—3.8	5.3 ± 0.1
Liters/min./sq.m.	3.7—2.1	2.9 ± 0.0
Liters/min./pound body weight	37—21	34 ± 1.

Normal range = mean ± two standard deviations.

cardiac output in liters per minute and the cardiac output per pound body weight and per square meter of surface area are presented. The values are in good agreement with those reported by others using this and other technics.

Table 2 compares the values of coronary blood flow obtained in two groups of patients matched for age and weight. One group was free from clinically evident cardiovascular disease. The other group was convalescing from myocardial infarctions. Total coronary blood flow is presented. The mean coronary blood flow and normal range are in good agreement with values published in the literature using other methods. Table 3 compares kidney blood flow determined by both the radioisotope method and the conventional para-amino hippurate clearance. Both right and left kidney blood flow are reported for the radioisotope method. The mean difference between these two methods was 4.2% and these two determinations had a correlation coefficient of + 0.735 ($p<.02$). While the mean value of the right and left kidneys are very similar, significant differences exist between the two sides. The correlation coefficient was + 0.403 which was not statistically significant.

Table 4 shows values of renal blood flow which were obtained from patients with various types of renal disease. Renal blood flow is reduced in all patients except for the patient with congenital hypoplasia of the left kidney.

TABLE 2

COMPARISON OF MEAN ± STANDARD ERROR OF MEAN OF CORONARY BLOOD FLOW IN PATIENTS WITH AND WITHOUT MYOCARDIAL INFARCTIONS

	Normal	*Post Infarction*
Number of subjects	19	9
Mean age	49 ± 2	50 ± 2
Mean weight	152 ± 1	150 ± 1
Coronary flow ml./min.	306 ± 18	161 ± 9
Normal range ml./min.	153—459	(mean ± 2 S.D.)

TABLE 3

COMPARISON OF RADIOISOTOPE AND PARA-AMINO HIPPURATE METHODS FOR DETERMINING RENAL BLOOD FLOW IN 10 NORMAL SUBJECTS

Radioisotope Method	*Ml./Min.*
Right kidney	514 ± 28
Left kidney	538 ± 34
Total	1,051 ± 50
Para-amino hippurate	1,032 ± 62
Mean per cent difference	4.2

Discussion

Of the radioisotope methods available only the method presented here and the radiocardiogram are capable of giving quantitative estimates of blood flow without the need of catheterization.[5-8] This is possible because the area of a time activity curve determined during the first circulation is proportional to blood flow. If we can assume complete mixing of the tracer as it passes through the heart and lungs, the amount of the tracer injected into each organ must be proportional to the blood flow. Using the formula developed here, the injected portion can be determined and from this organ blood flow calculated.

Others have shown that cardiac output measured by this method correlates well with values obtained by the direct Fick procedure.[7,8] Because this method lends itself to repetition and does not require arterial sampling, it is useful in routine clinical studies.

The renal blood flow values obtained by this method have been compared in 9 patients without known renal disease with those obtained by para-amino hippurate clearances performed simultaneously. A statistically significant correlation was found between the two methods ($r = 0.735$ $p<.02$). However, no correlation of significance statistically was obtained between right and left kidney blood flow. The method reported here has the advantage of being simple, not requiring catheterization and being applicable in patients

TABLE 4

RENAL BLOOD FLOW VALUES IN RENAL DISEASE

Disease	*Right*	*Left*	*Total*
Chronic glomerulonephritis	288	280	568
Chronic pyelonephritis	271	171	442
Nephrosclerosis	184	239	422
Malignant hypertension	332	109	441
Malignant hypertension	100	397	497
Congenital hypoplasia	189	815	1,004
Normal range (mean ± S.D.)	328—724		733—1,369

with renal tubular dysfunction. It has the further advantage of allowing one to estimate individual kidney blood flow. The patients with renal disease presented here have had values of renal blood flow below those of the normal group, showing that differences can be demonstrated between normal and abnormal renal blood flow. As in the iodine-131 Diodrast excretory test of Winter,[10] this method should be useful in the measurement of unilateral renal disease.

The measurement of coronary blood has been a highly technical procedure requiring intracardiac catheterization. This has seriously limited the use of this potentially valuable determination. The method presented here circumvents this difficulty. It clearly separates patients with myocardial disease from the normal and can be used in seriously ill patients.

The procedure we have presented is simple to perform. However, to obtain good results, certain technical considerations must be borne in mind. The size of the crystal for the heart channel must be large enough to include the outflow tracts of the heart but not so large that it includes too great a portion of the thoracic vessels. Too large a crystal produces an equilibrium value which is relatively too high to be used with the heart curve. The sensitivity of the different channels and the dose of radioactivity must be carefully balanced so the peaks of the heart curve reach at least 7,000 counts per minute, and kidney must not be greater than 3,000 counts per minute. If the radioactive dose is near the threshold of the sensitivity of the instrument, the heart peak will not be high enough to allow the coronary blood flow to be readily ascertained. If on the other hand, the dose is too great, skin, muscles and other organs may appear in the tracing and mask the kidney curve. A fast time response in the ratemeter is necessary to keep it in phase with the radioactivity in the blood stream. This produces a very irregular curve but one that can be accurately measured. With careful attention to detail, all of these technical difficulties can be easily overcome.

Summary

A radioisotope method has been presented which allows one to determine cardiac output and peripheral organ blood flow.

The technical design, graphical analysis and mathematical calculations have been described. Normal and abnormal values for coronary and kidney blood flow have been presented. This method is applicable to routine clinical testing.

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Discussion (Abstract)

Dr. Jack G. S. Maxfield, Dallas, Tex. The excellent paper by Drs. Sevelius and Johnson further substantiates our long held faith in the value of radioisotopes. We feel that the use of radioisotopes in diagnostic procedures is limited only by the ability of the investigator to state properly the problem, the ingenuity of the investigator to select procedures to transform the tracer information into a form that is subject to clinical evaluation, and the ability of the electronic instrument to supply the data.

I want to call attention to the ever present need for adequate evaluations on normal individuals, followed by evaluations of known diseases of various categories, so the tracer responses and resultant curves can be standardized and readily recognized. The proper standardization of all radioisotope technics cannot be overemphasized.

The approach presented in this paper indicates a simplification and broadening of our ability to determine blood flow in a peripheral organ. I believe that this technic will earn a rightful place in our diagnostic armamentarium. I want to compliment the authors on maintaining as much simplicity as possible in this procedure while attempting to get the ultimate in information.

Intussusception of the Rectal Mucosa:

A Common Cause of Rectal Pain*

O. J. POTTHAST, M.D., *San Antonio, Tex.*

The author describes the recurrent bouts of severe pain referred to the rectum which he has found to be the result of prolapse of the rectal mucosa. He describes his method of treatment.

PAIN AND THE ABNORMAL DISCHARGE of blood from the rectum are the main reasons for patients presenting themselves to the physician for rectal examination.

This paper deals with a specific kind of pain in the rectum, now commonly called *Proctalgia Fugax,* since the term was first applied by Thaesen[1] in 1935. Previously it was called rectal neuralgia, rectal neurosis or rectal spasm.

This paper was started because of the emphatic insistence of a medical colleague whose wife was relieved of years of suffering from frequent severe prolonged attacks of this type of pain. She had been examined by several excellent physicians skilled in their specialty. Some told her that her trouble was nervous tension, others were noncommittal and one read her an article on proctalgia fugax, explaining that though the condition was well-known, the cause was not understood, nor was there any known treatment therefore.

In preparing this paper eighteen treatises on rectal diseases, several encyclopedias of medicine, works on treatment and the Transactions of the American Proctologic Society were reviewed. Also information was obtained from the W. F. Prior Company whose staff made a search of the world's literature on rectal pain.

It is of interest to go back into the known history of this condition. Pennington had a chapter on "Neuralgia of the Rectum" in his book printed in 1923. He stated, "The affection was first described by Hard of England in 1841 and soon after by Gray, also of England; the next year by Eitner of Germany and in 1843 by Simon of France. Since then it seems to have attracted little attention, and that mostly in works on nervous diseases, the treatises on Proctology being, as a rule, silent on the topic." Other authors more or less described the pains but considered them due to reflexes from known organic diseases or due to tabetic crisis. Up to the middle nineteen-thirties, when syphilis was more prevalent, unexplained rectal pains were described as due to tabes dorsalis. In my 43 years of practice I have never seen such a case of proctalgia. Probably the cases described as being due to tabetic crisis were cases of proctalgia fugax in tabetics.

Clinical Picture

Proctalgia fugax, meaning a rectal pain of short duration, is variously described by patients as a cramping, burning, cutting, agonizing colic-like pain in the rectum lasting from a few minutes to occasionally an hour or more; usually leaving the patient prostrated for a period of time. The pain varies in severity in different individuals from a dull ache to such severity that the patient writhes in pain. Usually he or she is awakened with it from a sound sleep. Then again it may follow an unusual strain, exertion, mental fatigue, the sexual act, or it may occur at any time without warning. In some the onset is with a sudden desire for defecation at an unusual time; upon reaching the commode the pain moves higher in the rectum and is associated with severe prostration, breaking out in a cold sweat and fainting. Others describe a sudden onset deep inside the rectum. Most say it feels like a severe cramp or spasm. Usually the pain gradually subsides after a variable time, perhaps a few minutes or occasionally after several hours. It may be so severe as to require an opiate for relief. The pain may subside and then recur with varying intensity during the at-

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tack. These attacks occur at varying intervals, sometimes years apart and again may occur every few weeks or days. Usually patients, in whom the attacks come on frequently, have become tense, nervous and fearful of a serious lesion, especially cancer.

From the literature it would appear that men are affected most often, but in my experience by far the greater number of cases occur in women, probably because most of my patients are women.

Some state they get ease during the attack by holding themselves in various positions until the attack wears off. Others use applications of heat, or fill the rectum with air or water. One of my medical colleagues never travels without his syringe so he can fill his rectum with water to relieve an attack, theorizing that he was washing away a small bolus of feces caught between his internal and external sphincters as the cause of his rectal spasm. Yet the syringe nozzle is always easily introduced, which would not be the case if the sphincters were in a spasm. Many persons seem to have such pain at various times, but the intervals between attacks being variable and far apart the pain is usually ascribed to something they ate, a laxative or a hemorrhoid which has subsided. Several of my patients, seeking relief for other conditions, never mentioned the rectal pains until they were specifically asked about pain in the rectum. When relieved of the condition they were among the most grateful.

We must remember that pain is a variable factor, varying in different individuals with different pain thresholds: Witness the occasional patient with ulcerated fissures who comes in because of rectal bleeding and yet complains of no pain though the base of the ulcer may expose the external sphincter.

That the condition is due to tension and neurosis is untenable because it occurs just as frequently, in my experience, in the stoical well-adjusted individual as in the nervous tense type, though after many attacks they usually are nervous and tense. One such stoical individual described his symptoms as follows: "There occurs a feeling as if I have to go to stool then there is a sudden stoppage, like that of a loose cork in a jug from which water was being poured suddenly lodging in the neck of the jug." With this he described just a dull ache. This man had no severe pain, yet he had the same condition which in other individuals causes severe prostrating pain.

From the descriptions given by patients and seeing the patients during an attack one naturally feels there must be a severe spasm of some type to cause such pain, yet examination during the attack reveals no spasm, as first noticed by Thaesen[1] in 1935 and later by Bolen.[2] I, myself, have had the opportunity of examining two such patients during the attack and verify that no spasm could be found.

In 1949, while interrogating a patient she suddenly grimaced and gasped that she was having the rectal pain. I almost picked her up bodily getting her on the table for examination. In the Sims' position nothing could be felt by the examining finger. Quickly inserting a large anoscope the rectal mucosa was seen to be intussuscepted. A large cotton tipped applicator easily reduced the intussusception with relief to the patient. The mucosa was very redundant and congested. In the inverted position proctoscopic examination revealed normal smooth rectal walls with slight congestion of the mucosa.

Having had under my care at various times several patients who gave a history of these rectal pains usually occurring at night, and awakening them from a sound sleep, I was at a loss to account for this. Repeated examinations were done. Proctoscopic study in the inverted position was always normal. Examination in the Sims' position showed in all a comparatively lax sphincter and a markedly redundant lax rectal mucosa freely mobile when manipulated with a cotton tipped applicator. It was postulated that probably this loose mucosa intussuscepted upon itself at times and thereby caused pain. If this were true, treatment which would cause adhesion of the mucosa to the muscular wall of the rectum should relieve the condition. It was several years before the opportunity occurred to examine a patient during an attack, and satisfying myself that the condition was due to intussusception of the rectal mucosa.

There can be well-grounded argument that intussusception of the rectal mucosa cannot cause such pain. Reviewers of the nerve supply of the rectum and anal canal have stated that the rectal wall above the

papillae of Morgagni is entirely insensitive to pain, and that it is not possible for any lesion which involves the rectal wall without extension into the adjacent pelvic viscera to produce pain. A rectal polyp may be destroyed by cauterization without the use of anesthesia. This is a well-known fact in the experience of any physician with a large proctologic practice. But, in my experience, if the polyp is pulled upon with a tenaculum thereby pulling on the submucosa, the patient has pain. This is comparable to operating upon other parts of the intestinal tract under local anesthesia. Only the abdominal wall is anesthetized, yet the intestines can be handled gently and resected by use of the cautery without pain. However, when the cauterization extends into the mesentery, or the mesentery is pulled upon, there occurs severe colic-like abdominal pain without localization.

The occurrence of intussusception of the rectal mucosa by its very nature must cause a pull or strain on the branches of the superior and middle hemorrhoidal vessels and the posterior attachment of the rectum which, after all, is but an extension of the intestinal mesentery, thus affecting the rectal nervous innervation. The sympathetic nerves to the rectum come from the inferior mesenteric plexus through the superior hemorrhoidal nerves and their plexuses distributed with the superior hemorrhoidal vessels, and branches from the hypogastric plexus accompanying the middle hemorrhoidal vessels. Also, cerebrospinal fibers from the second, third and fourth sacral nerves join the pelvic plexuses and enter the sides of the rectum. From these anatomic facts it is understandable that irritation of the sympathetics cause the severe colicky spasm-like pain and irritation of the cerebrospinal fibers from the sacral nerves give the localization of this pain.

Diagnosis

In the diagnosis of the condition all other causes of pain in this region must be considered and excluded. First, it is necessary that a careful history be taken and evaluated. Then should follow a physical examination and laboratory study as indicated, the least being a urinalysis, and finally a rectal and sigmoidoscopic examination. Hemorrhoids, fissure, fistula-in-ano, ischiorectal and pararectal abscess, prostatitis (in men), rectocele, cul-de-sac hernia or enterocele, pelvic diseases and factitial proctitis (in women), coccygodynia and the Thiele syndrome, sigmoidorectal intussusception, sacro-iliac and iliolumbar ligament relaxation, tumors contiguous to, and in the rectum, and tumors or cysts involving the cauda equina must all be considered and excluded. Often one of these conditions complicates the picture and, being most obvious, treatment is directed to it and later, after successful treatment or operation, the patient's complaints continuing reexamination reveals the redundant rectal mucosa. This has happened to me.

The diagnosis of hemorrhoids is obvious but nevertheless careful examination is necessary to exclude other conditions. They are the most common complication.

Anal fissure is usually accompanied by a tight anal sphincter and sphincter spasm. No case of a tight anal sphincter can be recalled as accompanying proctalgia fugax. But such conditions could exist.

Fistula-in-ano, ischiorectal and pararectal abscess are usually easily excluded.

The dull often thobbing ache of prostatitis with the finding of this tender swollen organ should cause no serious diagnostic difficulty.

Rectocele often accompanies instances of redundant rectal mucosa and, if moderate, is usually relieved by the treatment because of the resulting induration beneath the rectovaginal septum.

Enterocele may cause a dull, full aching pressure sensation in the rectum due to herniation through the cul-de-sac of Douglas. Here the recumbent position usually relieves the discomfort.

Diseases of the reproductive organs and pelvic inflammatory disease has to be considered. Factitial proctitis causes a dull, sometimes sharp, severe ache and rectal bleeding. The characteristic ulcer on the anterior rectal wall contiguous to the cervix, with the history of radium therapy to the cervix, should not be difficult to differentiate.

Coccygodynia and the Thiele syndrome simulate proctalgia fugax, especially the latter. The mobility of the coccyx is determined by means of the finger in the rectum and the thumb over the coccyx. If pain is caused by pressing inward on the coccyx the trouble is

usually relaxation of the sacrococcygeal ligaments and injections of anesthetic solutions into these ligaments relieves the complaint. If pressing outward on the coccyx produces pain there is also, in my experience, spasm of the levator ani, coccygeus or pyriformis muscles, with pains described as being inside the rectum and often accompanied by pains over the sacrum and gluteal regions which may radiate down the back of one or both thighs and legs. This is the Thiele syndrome. Here massage of these painful spastic muscles affords relief.

Sigmoidorectal intussusception, as so ably described by Granet,[3] often gives similar symptoms and is easily confused with proctalgia fugax; and apparently, in my experience, the incomplete form is a fairly frequent accompaniment. Some proctologists believe that sigmoidorectal intussusception is the cause of proctalgia fugax *per se*. Here the sigmoid intussuscepts into the rectum either completely, in the severe cases, or incompletely, where only the mucosa of the lower sigmoid is involved. The latter seems to be more frequent. In sigmoidorectal intussusception there occurs pain and straining at stool. Often only a small amount of feces is passed with the sensation of more needing to be passed, causing pain and straining often with evacuation of only blood stained mucus, the patient finally relaxing because of exhaustion. All gradations of these symptoms are found, mild to severe. In some cases the intussuscepted sigmoid may be felt by digital examination. Proctoscopic examination in the Sims' position usually reveals the condition. In rare cases examination has to be made with the patient standing. Seldom can it be seen in the inverted position. I believe the proctalgia of children is due to this condition.

At the time of the writing of this paper I am treating 2 women for intussusception of the sigmoid mucosa into the rectum by injection, like that given for the redundant rectal mucosa, with apparent improvement, though it is too early to evaluate the results. After the proctalgia fugax symptoms subsided in these 2 cases the symptoms of incomplete evacuation due to sigmoidorectal intussusception became apparent. Interestingly one of these patients comments most enthusiastically upon her relief of vague gastrointestinal distress and indigestion.

Relaxation of the sacro-iliac and iliolumbar ligaments which causes sacral backache with pains in the thighs and legs, and sometimes with aching inside the pelvis, must be considered. In one case this condition was predominant. Upon relief, after injection of these ligaments with proliferant solutions, the proctalgia became predominant. Previously, the pains caused by the relaxation of the ligaments and the proctalgia were thought to be the same by the patient. Upon relief of the proctalgia she called attention to the sensation of the incomplete evacuation. Examination now revealed intussusception of the sigmoidal mucosa into the rectum. She is the second patient in whom injections under the sigmoidal mucosa are being given.

Tumors or cysts in the lower part of the spinal canal may cause confusing pains and paresthesias. In two such cases I have found no redundant rectal mucosa.

In all cases of true proctalgia fugax there is a very redundant mucosa of the rectum hanging loosely from the rectal wall as seen during proctoscopic examination with the patient on the side in the Sims' position. However, it must be remembered that not all patients having redundant rectal mucosa have proctalgia fugax. Also, for that matter, after successful treatment causing enough adherence of the rectal mucosa to the muscularis to prevent mucosal intussusception, there is still some mucosal redundancy. But in all cases of proctalgia fugax there has been redundant lax rectal mucosa, and all patients have been relieved (one for nine years) after treatment to cause areas of adhesion of the rectal mucosa to the muscularis.

(Space does not permit of case histories.)

Treatment

Treatment is given with the patient in the inverted position using a medium length proctoscope and a long shanked needle, long enough to reach easily through the proctoscope. Injections are made in line posteriorly, anteriorly, and on each side at weekly intervals. Injections are started just below the rectosigmoidal junction and, as the proctoscope is withdrawn, injections are made under the mucosa approximately one inch apart. Care is taken not to completely en-

circle the rectum with the injected solution because of the theoretic possibility of resulting fibrosis causing later stricture. The solution used most often has been 5% phenol in almond or cottonseed oil. Approximately 1 cc. is injected at each puncture site, using as much as a total of 10 cc. per treatment. Four per cent phenol in equal parts of water and glycerin has been used, injecting about 0.5 cc. at each puncture site and using up to a total of 5 cc. With this there is less tendency to bleeding from the punctures. This solution seems to work equally as well as the oily solutions, though there is more chance of formation of a mucosal slough should the solution be injected inadvertently into the mucosa similar to an intradermal injection. The patient is kept in the inverted position until any and all bleeding from the needle punctures has stopped. The table is then elevated to the horizontal position, the foot piece raised and he is kept prone on the table for several more minutes before getting up.

Distention of the submucosa by the injections causes more or less pain, usually like that of the attacks of the proctalgia but lasting only a short time and ordinarily requiring no medication. In one severe case the patient invariably suffered the severe proctalgia fugax pains. She required 20 to 25 mg. Demerol intravenously for relief. This dosage of Demerol given intravenously was sufficient and did not depress the patient so she was able to leave the office after a short rest. This patient also required a narcotic taken orally several hours following each treatment.

The best solution for injection has, in my opinion, not been discovered up to this time, but apparently any solution used for the gradual sclerosing of hemorrhoids, provided it is strongly antiseptic, should be satisfactory for these treatments. I fear quinine preparations for these treatments because of the occasional systemic reactions which occur, and too large an amount would be necessary. Other mixtures and preparations have been tried but so far the phenol preparations mentioned have been the more satisfactory.

The treatment described is based on the result of successful treatment of rectal prolapse in children and the aged, where operation was contraindicated, and in one very severe case in an otherwise healthy middle-aged man who absolutely refused operation.

The relief of acute attacks of proctalgia fugax, as reported by some authors, with the inhalation of amyl nitrite or the taking of nitroglycerin under the tongue is hard to explain. It is generally conceded that the nitrites relax smooth muscle spasm, but their major effect is dilatation of the arterioles. Theoretically the relief obtained may be due to arteriolar dilatation and depression of the sympathetics relieving the pain until the mucosal intussusception reduces itself. Other writers have reported indifferent results from this medication. I have had no experience with its use. It should be tried when the physician is not equipped to give definitive treatment.

Summary

Since 1949, when intussusception of the rectal mucosa was observed during an attack of pain commonly called proctalgia fugax, the author has successfully treated these patients by the injection of fibrosing solutions under the rectal mucosa, causing adhesions of the mucosa to the muscularis of the rectum. The diagnosis and treatment of the condition is explained. Search of literature found no such previous explanation of the condition nor treatment for its permanent relief.

Attention is called to the cause of a proctalgia, which may be mild or severe, its recognition and treatment. Apparently it is quite common. If the physician is alert and searching in the taking of the history and aware of the condition when making the examination, he will be surprised to find many patients complaining of this affliction.

The author believes that his observations and the results of treatment have cleared away one more of the so-called idiopathic, neurotic and psychosomatic pains, as proven by the results of 22 cases in the past 9 years.

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Operation for Correction of Protruding Ears*

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Abnormalities of the external ear are commonly sources of distress for those so afflicted. Frequently such persons wish an operation for cosmetic reasons; in others there may be other reasons. In any event the author believes operation is justifiable for several reasons.

PROTRUDING EARS are quite common. A cursory review of the literature does not reveal any statistics of incidence, but protruding ears are probably the most common congenital deformity of the external ear. A protruding ear is usually an abnormally large ear (macrotia), and it is often this combination that brings the patient to the surgeon (Fig. 1). The upper portion of the auricle may be displaced outward and downward (dog ear or flop ear) or the superior crus may extend vertically with absence of the helical rim (satyr ear). Coexisting deformities of the lobule may also occur.

Protruding or abnormally large ears are the object of jest at any age, and often of sarcasm or satire. Children with such abnormalities are teased by their playmates and children can unintentionally be unmerciful in their teasing. Such teasing results in personality changes, occasionally aggressiveness, or even bumptiousness, but more often shyness and retirement. Realistically, it is because of the patient's or parent's realization of this situation that the surgeon is consulted.

Becker[1] and Withers[2] have reviewed the historical development of surgical procedures for correction of protruding ears. It is worthy of comment that Diffenbach, in 1845, was the first to attempt a correction; and that Luckett, in 1910, was the first to point out that protruding ears had no antihelix and, to correct the deformity, the surgeon must create an antihelix. In later years there have been many excellent contributions by distinguished surgeons. Those interested in more details are referred to the reports of Becker and Withers.

It should be unnecessary to state that any surgeon interested in this field should know, in detail, the anatomy of the external ear. I see no reason to review it here.

The various anatomic deformities encountered explain the variations in the surgical procedures that have been employed for correction. It is obvious that each patient must be studied individually and that, rather than following any one type of surgical procedure, the principles of surgery that are applicable must be followed, adapting the operation to the case.

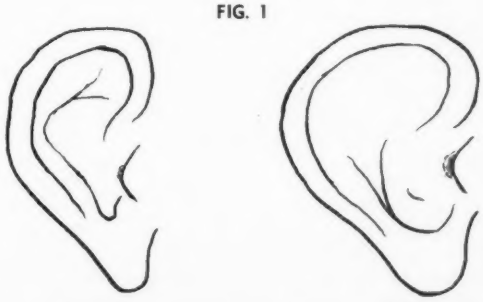
These surgical principles include:

1. Operation should not be performed until the ear is fully developed, which usually occurs at the age of 5 years.

2. The desired result is an ear that appears normal, and the reconstruction must be planned in advance.

3. The basic surgical principles for all elective

FIG. 1



Left, normal ear, compared with right, abnormally large protruding ear.

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The illustrations were taken, in part, from Berson's Atlas of Plastic Surgery, New York, Grune and Stratton. They are schematic diagrams and not accurate drawings of the operative procedure.

surgery must be observed: The patient must be in satisfactory physical condition, and the ear free of infection; adequate pre- and postoperative sedation, and adequate antibiotic coverage are prerequisites.

4. Local anesthesia is preferable for older children and adults. General anesthesia is necessary in young children, but the use of additional local anesthesia aids in hemostasis, and makes dissection easier. Cyclopropane is contraindicated by the use of epinephrine.

5. If the ear is too large, it is necessary to excise some skin from the postauricular area but an excessive amount should not be excised. A normal postauricular sulcus is desirable, and the ear should not appear "plastered" to the head postoperatively.

6. It is necessary to incise the auricular cartilage to break the spring of the cartilage, and form the new antihelix (and crura, when necessary). Even in normal sized ears, I think it best to excise a very narrow strip of cartilage; in abnormally large ears a wider strip must be excised, the width depending on the size of the ear. Abnormally large ears usually have an abnormally deep cavum concha, causing the lower portion of the ear to protrude laterally, and the excised strip of cartilage should include a strip of the posterior lateral conchal wall, medial to the posterior lateral margin of the concha.

7. The dissection of the cartilage should be carried out entirely from the posterior surface, without damage to the anterior skin surface. After the cartilage is excised it is necessary to dissect the anterior skin from the perichondrium along each margin for a distance of 3 to 5 mm., depending on the width of the excised cartilage. Such dissection should be gentle and the anterior skin surface should not be perforated.

8. The margins of the superior cartilage must be everted and sutured to form the new antihelix. When the strip excised is a very narrow one, external sutures may be preferable; these sutures should pass through the anterior skin surface and cartilage margins back through anterior skin, but should not pass through the posterior skin. When a larger strip is excised it is preferable to suture the everted margins with buried sutures. If cartilage was removed from the concha, the conchal cartilage margins are approximated, not everted, by buried sutures. Chromic gut 4-0 is preferable for buried sutures; 3-0 black silk should be used for external sutures, and when passed through cartilage must be tied over rubber or cotton.

9. Absolute hemostasis must be obtained before closing the incision. The postauricular incision is closed with interrupted sutures of 3-0 black silk.

10. Meticulous care must be observed in the postoperative dressing to obtain a good result. Sterilized gauze sponges are placed in the postauricular area to protect the postauricular and mastoid skin and hold the ear at a normal angle. Strips of gauze, moistened in 1:1,000 benzalkonium (Zephiran) solution and then squeezed fairly dry, should be carefully packed in the convolutions of the ear, to retain the dissected anterior skin in proper place and avoid hematomas. The external canal is not packed. A piece of foam rubber should be trimmed and placed around the margins of the ear to protect it from too much pressure. An Ace bandage should be applied with moderate pressure. This dressing should not be disturbed for 3 days. A lighter dressing can be used thereafter.

I would like to particularly emphasize the importance of the postoperative dressing being properly applied. Postoperative drains are not employed and postoperative hematomas must be avoided. This can be done best by complete hemostasis and gentle, careful postoperative packing, with a moderate pressure bandage.

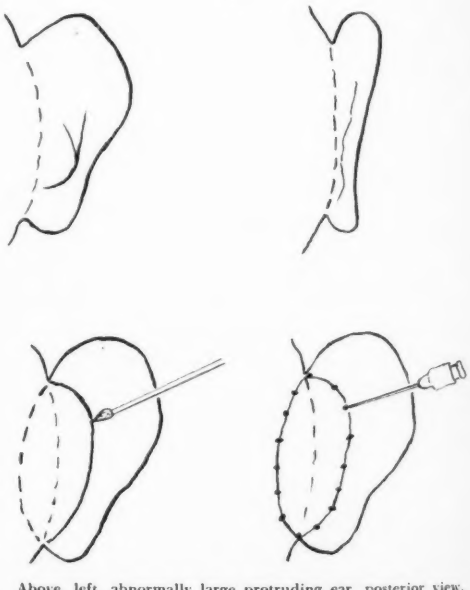
The technic employed in operating upon the two cases to be shown in the colored movie was:

1. The 13 year old girl was operated upon under local anesthesia, the 10 year old boy under general anesthesia,—vinyl ether (Vinethene) induction followed by ether.

2. The scalp was shaved for an additional inch around the top of the ear, and the hair restrained from the field with strips of Scotch tape. The field was prepared with ether, alcohol and 1:1,000 aqueous Zephiran solution.

3. The ear was carefully placed against the head in the desired position, and the line of contact marked on the posterior auricular surface with gentian violet. In my experience, a 20 gauge hypodermic needle dipped in gentian violet is quite satisfactory. Cotton tipped applicators, and any other dye, such as methylene blue or brilliant green, may be used. The auricle was then placed against the mastoid, the line of dye making another line on the mastoid skin, and this was more heavily outlined with the dye. In the case

FIG. 2



Above, left, abnormally large protruding ear, posterior view. Above, right, same ear, repositioned. Below, left, line of contact marked with dye. Below, right, hypodermic needle with dye used for prick-points in marking skin.

operated under general anesthesia, this line was immediately further marked by prick-points of the needle with dye. In the case operated under local anesthesia, the prick-points were made immediately after injection (Fig. 2).

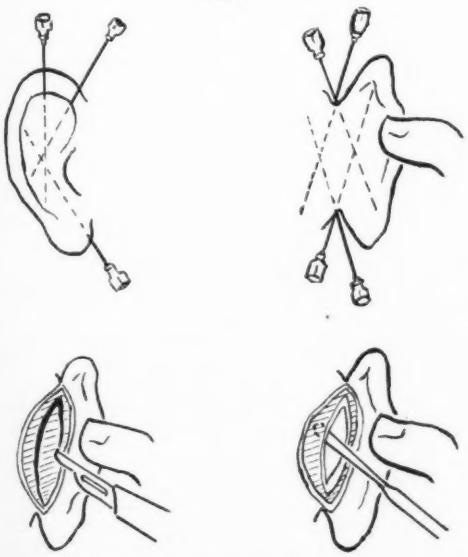
4. Lidocaine (Xylocaine) 2% with 1:50,000 epinephrine hydrochloride solution was injected in the anterior and posterior surfaces of the auricle, and in the adjacent mastoid area.

5. The ellipse of skin outlined on the posterior auricular and mastoid areas by the dye was then excised (Fig. 3).

6. An irregularly crescent-shaped piece of cartilage was then excised. The strip was outlined by two incisions through the cartilage along the line of the proposed new antihelix and superior crus, continuing downward to remove a portion of the concha. The anterior incision through the cartilage was approximately 4 mm. posterior to the anterior skin incision. Incidentally, one should be careful not to excise too wide a strip of cartilage. The narrowest strip that will give a good result is to be preferred. After excising the strip, the margins of the cartilage are approximated by being placed against the head to observe their positioning; and an additional strip of cartilage can then be excised if indicated.

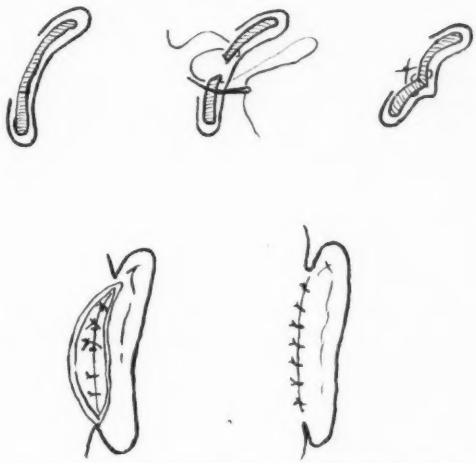
7. The anterior skin was then dissected free of the anterior perichondrium for a distance of approximately 5 mm. along each border. A Logan semi-sharp cleft palate elevator can be used, but I prefer the back tip of a Bard-Parker #15 blade and use sharp dissection when the skin is very firmly adherent. When sharp dissection is used, it must be used carefully to avoid damaging the perichondrium or button-holing the skin.

FIG. 3



Above, injection of anterior and posterior surfaces, and adjacent mastoid area. Below, left, an ellipse of skin has been excised and a strip of cartilage is being excised. Below, right, the anterior skin is being dissected from the anterior perichondrium.

FIG. 4



Above, left, cross section of upper cartilage of protruding ear; middle, strip of cartilage has been removed, cartilage margins beveled and a suture is being inserted to evert and unite margins of cartilage; right, antihelix has been created by everted cartilage margins. Below, left, shows sutures through cartilage; upper suture not tied tightly, to form superior crus; second and third sutures tied more tightly to form antihelix; bottom two sutures do not evert cartilage, simply uniting them to form a normally shallow cavum concha. Below, right, postauricular sulcus reformed, by uniting skin margins with interrupted sutures of black silk.

8. The cartilage margins that form the antihelix should be slightly beveled, but the conchal cartilage margins should be squared. In the cases shown this was done when the incisions were made, but at this stage the margins should be inspected and any indicated trimming done. There should be no ragged or irregular margins. The new antihelix was then formed by everting the upper cartilage margins with 3 sutures of 4-0 chromic gut. All sutures were placed before any were tied. The superior suture was not tied as tightly as the other two upper sutures, so that the superior crus would not be too sharp (Fig. 4).

9. At this point the field was checked for hemostasis. Hemorrhage had been negligible, but a few small blood vessels had been clamped with tiny hemostats. The hemostats were removed; bleeding points were again picked up and tied with 4-0 plain gut.

10. The postauricular incision was closed with interrupted sutures of 3-0 black silk.

11. The postoperative dressing was applied very carefully, as outlined above.

12. The pressure bandage was removed on the third day and replaced by a lighter, gauze bandage. The gauze bandage was discontinued on the seventh day and a cotton-collodin dressing applied. The sutures were removed on the tenth day.

Perhaps I should mention that some plastic surgeons have been concerned about the re-

sulting postoperative "sharpness" of the antihelix, and have employed various measures to avoid such a result. These measures include thinning of the auricular cartilage with knife or burr, cross-hatching, and multiple adjacent parallel incomplete incisions through the cartilage along the line of the antihelix, and inserting external sutures over rubber or cotton pads. It should be remembered that the antihelix and the inferior crus are normally fairly sharp. Only the superior crus is rounded. This result can be achieved by the described technic by removing only a very narrow strip in the region of the superior crus, and tying the superior suture only tight enough to form a prominence rather than a sharp edge. It is important that the margins be clean, linear and well defined; they must not be ragged.

Summary

Protruding ears are fairly common and often have an unfortunate effect on the patient's personality. The surgical procedure for the correction of this abnormality is a fairly simple one but certain principles must be observed to obtain a satisfactory result. These basic surgical principles have been presented. The surgical technic employed in the two cases shown in the colored motion picture film has been described in detail.

In *conclusion,* I join Withers in the opinion that an otolaryngologist should think no more of correcting protruding ears than an orthopedist does of correcting clubfoot, or an ophthalmologist does of correcting ptosis of the eyelids.

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Discussion (Abstract)

Dr. Richard T. Farrior, Tampa, Fla. It is a distinct pleasure to discuss Dr. Jones' paper on a subject in which I have been particularly interested. He has given a concise review of the problem, with many practical technical points, and, certainly has demonstrated that he has a keen understanding of both the psychologic and technical problems involved.

Any surgeon who is performing these plastic procedures of the ear should strive, as nearly as possible to mimic nature, and I would stress some attention at duplicating the natural contours of the ear as seen in the profile as well as in the anterior view. Perhaps the points I would make are minutiae, but the technic developed has been aimed at producing as nearly a normal contour as possible, and has given quite satisfactory results.

In the discussion, slides were shown of the detailed anatomy of the contour of the average, normal ear, stressing the acute angulation of the inferior crus and the gradual convexity of the superior crus in the area of the fossa triangularis. A horizontal section across the concha, antihelix proper, and scaphoid fossa emphasizes the definite prominence of the antihelix and grooved scaphoid fossa between this antihelix and the helical rim.

Kodachrome slides, using both line drawings and photographs taken of the actual surgical procedure, emphasize the following points in the technic: First, there are no definite through and through incisions about the entire superior crus which would be visualized from the anterior surface. Secondly, there is a definite break at the junction of the crura between the anterior margin of the superior crus and the excised cartilage about the conchal rim. I agree with Dr. Jones that this cartilage be excised in almost every case to effect adequate correction of the protrusion. With the sutures in place, so as to override the antihelix proper, and properly bend the superior crus, I believe we are obtaining more nearly normal contour in the average protruding ear. For the antihelix proper and into the superior crus, longitudinal parallel strips or wedges of cartilage are removed from the posterior surface of the auricle, not going through the full thickness of the cartilage. About the antihelix proper, cartilage is excised about the conchal rim and a third incision made paralleling the scaphoid fossa, leaving a strip of cartilage between, which can be sutured so as to override, forming a prominent antihelix. It would be emphasized again that these through and through incisions extend only to the level of the junction of the crura and that there are no through and through incisions about the superior crus.

The only other difference in technic that I would present is that the skin I excised is only opposite the antihelix itself, taken from the posterior surface of the auricle, no skin being excised from the angle or mastoid. With this incision, adequate exposure for the outline surgery is obtained, more assistance to the initial buckling of the cartilage is produced and a more natural auriculomastoid angle is effected.

In summary, the differences in this technic from existing technics are primarily,—a definite break between the conchal rim incision and the partial incision of the superior crus which gives a more natural fold in this area, the use of excised longitudinal cartilage strips to effect a gradual convexity in the superior crus, and more acute convexity inferiorly at the antihelix proper.

Again, I want to express my pleasure at having the opportunity to discuss this paper and to congratulate Dr. Jones on his very excellent movie. He has most ably demonstrated both the deformity and its correction, including the psychologic benefits.

Dr. Jack R. Anderson, New Orleans, La. It is indeed a privilege to be able to discuss Dr. Jones'

presentation. I must agree with him that every otolaryngologist should be performing this very simple procedure. It is a constant source of amazement to me to see men who daily do all types of intricate and delicate procedures through endaural incisions refer patients who desire otoplastic procedures to general plastic surgeons.

Dr. Jones has correctly emphasized the psychic trauma accruing to those children who have protruding ears; that this is a very real thing, I can vouch for on the basis of personal experience.

He did not mention that as the general public becomes more sophisticated about plastic surgery, an increasing number of otoplasties are being requested by adults. These people are variously motivated. There are men who feel that their protruding ears make them appear ludicrous, a condition not desirable in our highly competitive world where putting our best foot forward appearance—and otherwise is so highly desirable. Women often seek correction because prominent ears severely limit the types of hair styles or hats they can wear. Others request the operation because of economic or career considerations, as may be the case with actors, models, salesmen, or others whose jobs require them to meet and deal with the public much of the time.

Dr. Jones has wisely advised against slavishly adhering to one type surgical procedure. The most important thing is to know what is causing the deformity in question and adopt the operation to fit the case.

Foremost among the requirements for achieving success in otoplasty, whatever the technic, is that the spring of the cartilage be completely broken. At the conclusion of the operation, the ear should assume the desired position without the aid of sutures. The surgeon *cannot* depend on sutures, excision of skin, or the postoperative dressing to hold the ear in its new position. To do so is folly for, too often, the tensile strength of the cartilage will assert itself in several weeks and the deformity will recur. The two places where one is most apt to overlook breaking the spring are in the region of the cauda helicis and where the helical rim joins the inferior crus, just above the spina helicis.

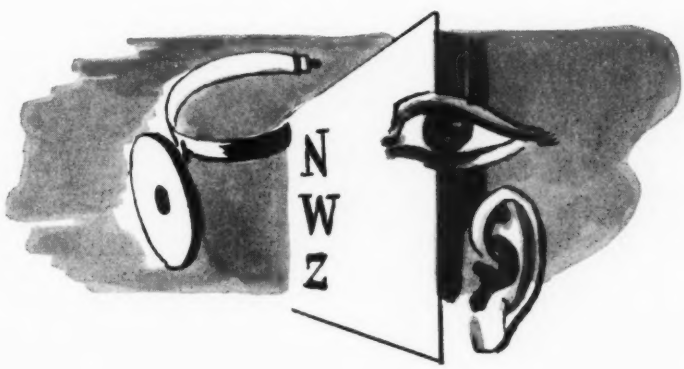
The less cartilage one must remove, the better. However, if removal of cartilage is necessary to achieve the desired correction, I feel it should be done.

Postoperatively, the administration of analgesics must be kept to a minimum so that they do not mask pain which is the sign of too tight a dressing or the development of a hematoma.

Following removal of the dressing on the fifth or sixth postoperative day, the patient should be advised to wear the top of a ladies' Nylon stocking over the ears while sleeping for a period of 2 weeks. This is not done to assure the maintenance of the new position but rather to avoid the possibility of traumatizing the ears when rolling over during sleep.

The percentage and degree of patient satisfaction is extremely high following otoplasty; certainly, it far exceeds rhinoplasty, for example. The mere fact that the scapha is moved more parallel to the side of the head serves to gratify and amaze most patients and their associates.

In conclusion, permit me to again thank Dr. Jones for permitting me to discuss his paper and congratulate him on his fine, lucid, and timely presentation.



CASE REPORT

Treatment of Procaine Amide Intoxication

PAUL L. RODENSKY, M.D., and
FRED WASSERMAN, M.D.,† *Coral Gables, Fla.*

THE SUCCESSFUL TREATMENT of quinidine and procaine amide intoxication has recently been reported both in the experimental animal and in man.[1-4] We wish to present another patient who developed procaine amide intoxication and was successfully managed with a combination of molar sodium lactate and L-norepinephrine.

Case Report

A 67 year old white man was first admitted to the Coral Gables Veterans Administration Hospital in Jan., 1958, for chest pain and palpitation. His past medical history was noncontributory. Except for mild cardiomegaly and a rapid regular apical rate of 170 per minute, the physical examination was within normal limits. An EKG. revealed an atrial flutter with 2:1 A-V block; the atrial rate was 340 per minute and the ventricular rate 170 per minute. There was no evidence of old or recent myocardial infarction. The patient was treated with digitalis and quinidine with prompt conversion to normal sinus rhythm. He was maintained on digitalis and quinidine until one month prior to the present admission when he discontinued these without consulting a physician.

The patient was readmitted to the hospital Sept. 22, 1958, for precordial chest pain associated with palpitation and mild dyspnea. Physical examination revealed a B. P. of 110/80 and an apical rate of 170 per minute. He appeared cold, clammy and in obvious acute distress. There were no signs of congestive failure. The heart was again noted to be slightly enlarged; there were no murmurs or rubs.

The laboratory findings were as follows: hematocrit 41%, Hgb. 14.5 Gm., WBC 11,350 with a normal differential. Urinalysis was unremarkable. The serologic test for syphilis was negative. The BUN. was 22 mg. %, sedimentation rate was 18 mm./hr. (cor.), the serum sodium was 135.5, potassium 3.7, CO_2 combining power 22 and chlorides 110 mEq./L. Serial serum transaminase levels were 59, 48, 36, 33, and 23.

Because of the rapid ventricular rate (170 per min.) the patient was digitalized with 1.2 mg. of intravenous lanatoside C without any effect on the rhythm (Fig. 1). Carotid sinus pressure before and after digitalization failed to increase the degree of A-V block. One hour after the intravenous administration of lanatoside C, intravenous procaine amide was started utilizing continuous electrocardiographic monitoring; 500 mg. of procaine amide was given at a rate of 100 mg. per minute. The atrial rate slowed to 300 per minute but the 2:1 A-V block persisted; occasionally, transient 3:1 A-V heart block was observed.

Immediately after the administration of procaine amide, there was marked widening of the QRS complexes from a control of 0.07 second to 0.14 second, and deep slurred S waves appeared. The patient's B. P., previously recorded at 110/80, fell to 88/58. It was thought the hypotension and electrocardiographic changes were manifestations of procaine amide intoxication. L-norepinephrine, 8 mg. in 1,000 cc. 5% glucose in distilled water, was started and the B. P. was maintained at approximately 110/80; the electrocardiogram continued to show widened distorted QRS complexes. Twenty-five milliequivalents of molar sodium lactate were given intravenously over a 5 minute interval, and within 5 minutes after administration the QRS complexes had returned to normal duration and configuration (Fig. 1, H). L-norepinephrine was discontinued and the B. P. remained stable at 110/80. Subsequently, carotid sinus pressure easily produced an increase in the degree of A-V heart block. With an additional 0.4 mg. of intravenous lanatoside C, 3:1 A-V nodal block became established, and the patient improved symptomatically as a result of the slower ventricular rate (100 per min.). The following morning the patient was observed in atrial fibrillation with a ventricular rate of 75 per minute (Fig. 2). After 3 doses of quinidine sulfate by mouth (0.2 Gm. every 6 hrs.) he converted to a normal sinus rhythm. He has remained in a normal rhythm on maintenance doses of digitalis and quinidine sulfate. Except for the slight elevation of two serum transaminase determinations there was nothing clinically, electrocardiographically or in the other laboratory studies to support the diagnosis of myocardial infarction (Fig. 3).

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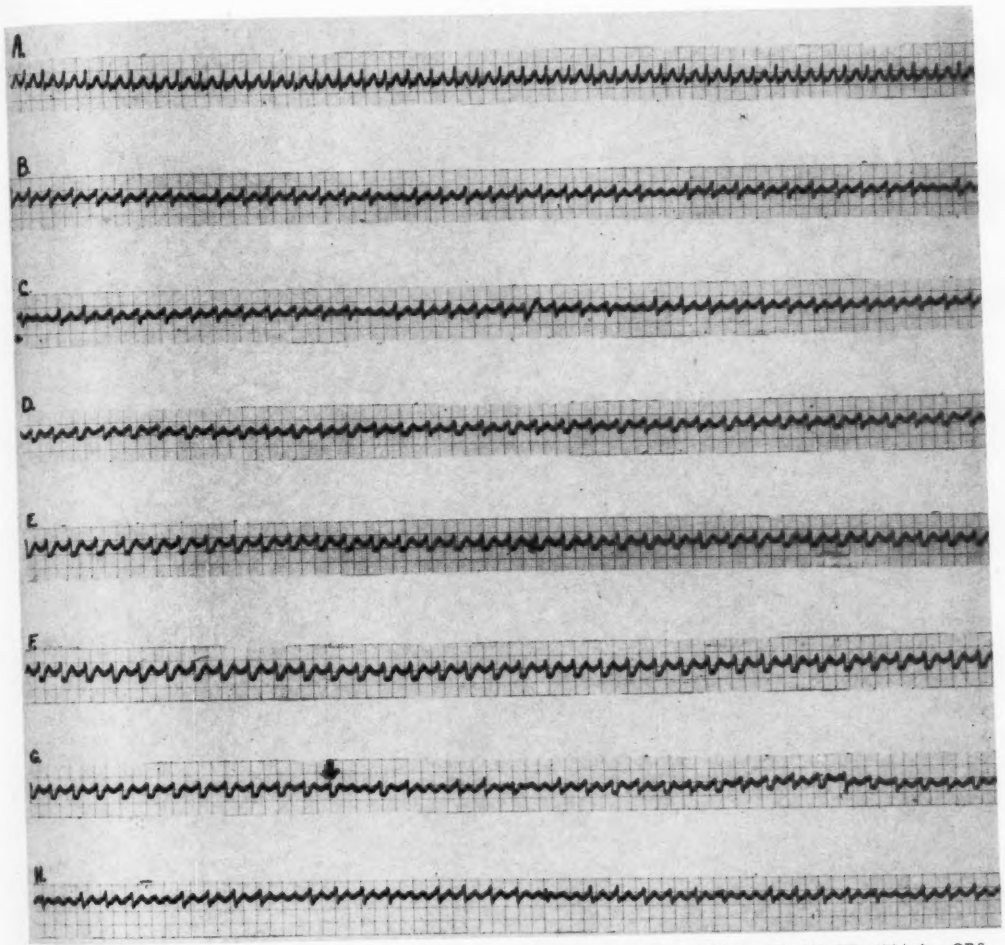
Discussion

Procaine amide is one of the newer therapeutic agents enjoying wide usage in the management of ectopic rhythms.[5-8] It has been advocated for the treatment of various arrythmias including atrial flutter, fibrillation, premature atrial, nodal and ventricular contractions and ventricular tachycardia.

Much has been written about the effects of procaine amide on the heart.[9,10] It delays impulse conduction in auricular muscle, the bundle of His and ventricular muscle. Along with this slowing of conduction, resulting from an increase in the refractory period of auricular muscle, myocardial irritability is generally depressed. In addition, there is a transient vagolytic action.

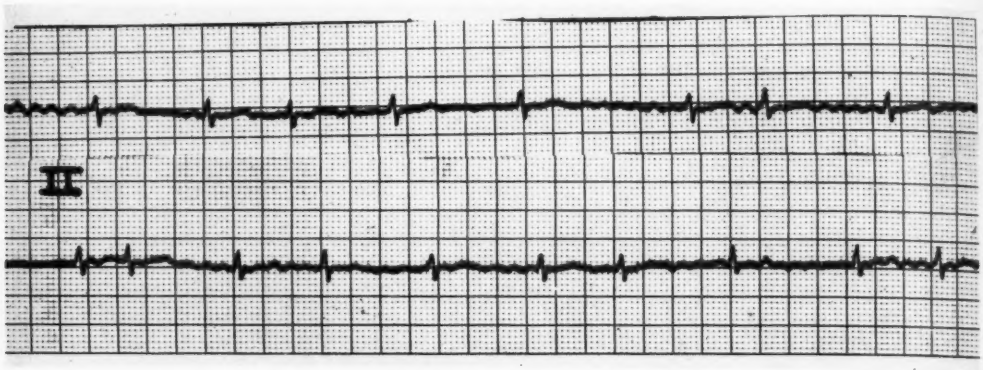
When given orally procaine amide is rapidly and almost completely absorbed with a peak plasma level occurring in 2 hours. With intramuscular administration the maximum

FIG. 1



(A) Control lead II, after 1.2 mg. lanatoside-C I.V., showing atrial flutter with 2:1 A-V block; AR=340, VR=170/min.; QRS complexes measure 0.07 second in duration. (B) After 200 mg. procaine amide I.V. in 2 minutes, atrial rate now 330 with occasional 3:1 block. There has been no change in QRS duration. (C) After 300 mg. procaine amide I.V. in 3 minutes. (D) After 450 mg. procaine amide I.V. in 4½ minutes, the atrial rate has slowed to 300/min. with QRS widening observed in alternating complexes. (E) After 500 mg. procaine amide in 5 minutes, the QRS complexes have widened to 0.14 second and there are deep notched S waves. (F) After 5 cc. of molar sodium lactate I.V. in 2 minutes. (G) After 25 cc. of molar sodium lactate in 5 minutes in combination with L-norepinephrine, there is transient 3:1 A-V nodal block and narrowing of the QRS complexes. (H) 15 minutes after 25 cc. of sodium lactate; L-norepinephrine has been discontinued. There is transient 3:1 A-V block; the QRS complexes have narrowed to 0.07 second in duration and returned to a control configuration.

FIG. 2

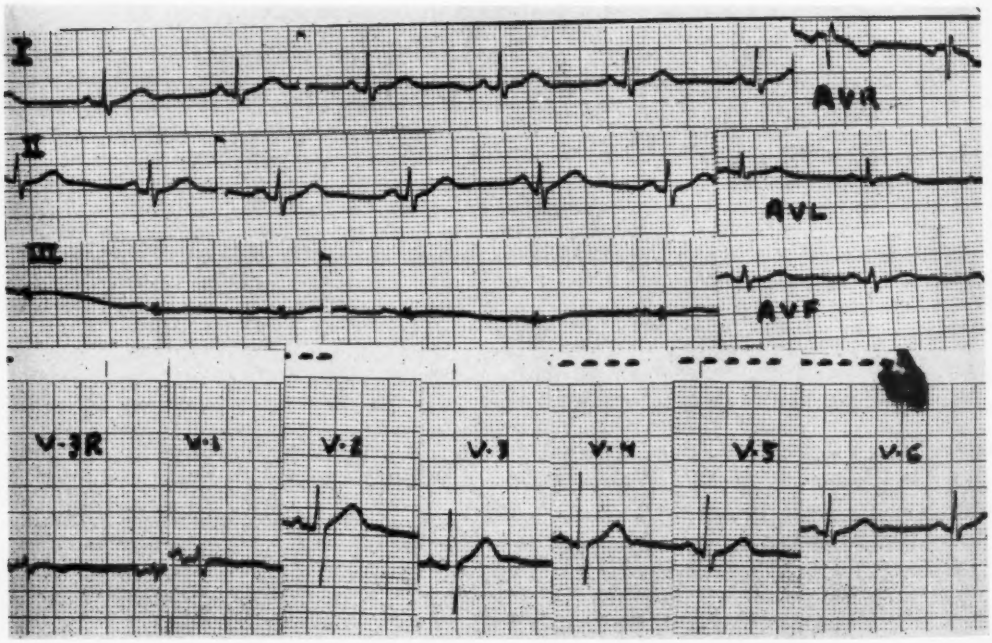


Long lead II showing conversion to auricular fibrillation.

action is obtained in 30 to 60 minutes. After reaching a peak the plasma level declines at a rate of 10 to 20% per hour.[6] With the intravenous administration of procaine amide the maximum effect is observed within 4 minutes.[9]

The cardiotoxic effects of procaine amide include intra-auricular conduction defects, an increase in the P-R interval and widening of the QRS complexes with notching, which resembles an indeterminate type of bundle branch block. Hypotension has also been observed. Severe procaine amide intoxication produces atrioventricular dissociation, a slow nodal or idioventricular rhythm and ultimately ventricular standstill or fibrillation.[8]

FIG. 3



EKG. prior to discharge showing normal sinus rhythm and an incomplete right bundle branch block.

Until recently there has been no method of treating procaine amide intoxication other than cessation of therapy.

With the demonstration that molar sodium lactate was efficacious in narrowing abnormally widened QRS complexes due to various causes,[11,12] experimental work was undertaken to explore the effects in quinidine and procaine amide intoxication.[1,2,4] It was subsequently demonstrated in the experimental animal that molar sodium lactate alone and in combination with L-norepinephrine reversed many of the cardiotoxic effects of procaine amide and quinidine. The application of these experimental findings in the successful treatment of 3 patients with varying degrees of quinidine and procaine amide intoxication has been reported elsewhere.[3] The precise mechanism action is not clear, but may result in part from the ionotropic effect of L-norepinephrine on the myocardium and the alkalosis (or decrease in existent acidosis) rather than simply the pressor effect and the previously reported effects of hypertonic sodium lactate on the heart.

Summary

A case of procaine amide intoxication is reported. The efficacy of molar sodium lactate used in combination with L-norepinephrine in reversing the hypotension and conduction defects produced by procaine amide is demonstrated.

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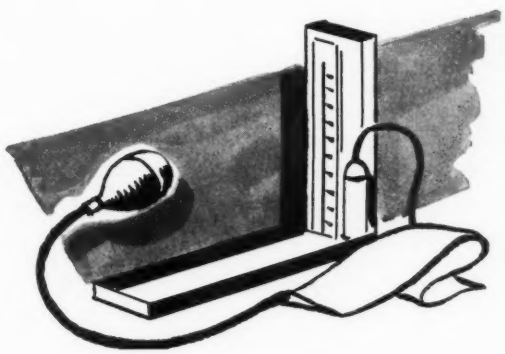

Micturition Syncope: Report of Two Cases

ROBERT RAY McGEE, M.D., *Clarksdale, Miss.*

These cases are of exceeding interest in that they point to a physiologic phenomenon which may not be uncommon, but has not been generally recognized, or at least not mentioned in the literature until very recently. That this should be so is amazing.

THE AUTHOR WAS MYSTIFIED recently by the case of a young man whose chief complaint was fainting during urination. A search of the standard reference texts did not reveal mention of such an association. The 1945 edition of *French's Index of Differential Diagnosis*[1] lists over 100 situations giving rise to fainting attacks. Aside from the expected causes, such as hemorrhage, hysteria and cerebrovascular attacks, there are listed such fascinating causes as loathsome smell, unkind words, horrible spectacle, flatulence, and finally simple faints without apparent cause. In this long list there is no mention of fainting associated with the act of micturition.

Since the above patient was seen, two reports have been published describing syncope during micturition. Dermksian and Lamb,[2] in a general discussion of syncope in healthy young adults, describe four instances of this association in a study of 113 syncopal episodes in 82 individuals. Proudfit and Forteza[3] in a recent article report 7 cases of micturition syncope.

A second patient has since been seen with this syndrome and the two cases are presented below.

Case Reports

Case 1. J. S., a 32 year old white man, was seen on Sept. 22, 1958. Two nights previously, after having drunk three cans of beer and having a very full bladder, he suddenly fainted while voiding. This episode was observed by a cousin who stated that the patient suddenly slumped to the floor and was unconscious for about a minute or two. There were no involuntary movements and no tongue-biting. Immediately after fainting he was observed by his wife, a medical technician, who stated that he appeared very pale but otherwise not remarkable. Afterward he was asymptomatic except for a feeling of mild weakness.

On further questioning, he stated that on two other occasions during the past 5 years he had had similar episodes while voiding. On both of these previous occasions he had been asleep and had been awakened suddenly and gone to the bathroom to void. Both attacks were exactly like the present episode. There was no history of fainting at any other time. The review of systems was entirely negative. There had been no past serious illnesses and no operations other than tonsillectomy. The B.P. was 120/80, the P. was 88, the T. was 99°, and the respiration was 18. A general physical examination was entirely negative. Routine urinalysis and routine blood counts were normal.

Case 2. R. T., a 22 year old white man, was seen on Feb. 17, 1959. He had awakened the previous morning with headache and malaise and during that day developed a sore throat. The morning of the 17th, immediately after awakening, he got up out of bed to urinate and fainted during urination. He was unconscious for perhaps a minute and afterward felt all right except for persistence of the sore throat and malaise. The review of systems was entirely negative. There were no urinary tract symptoms.

Two years previously he had also fainted on two occasions during urination immediately after arising from recumbency as in the present instance. At that time he was seen by a physician who told him he had "pus on the kidneys" and he was treated for this. There had been no recurrence since that time. He had never fainted on any occasion except the three times described. Physical examination revealed a B.P. of 110/60, a P. of 76, and a T. of 99.4°. Examination was otherwise entirely negative except for a mild diffuse pharyngitis and mild nasal congestion. Routine urinalysis was negative.

Comment

As pointed out by Dermksian and Lamb[2] a great variety of clinical incidents may precipitate syncope. However, until recently the occurrence of syncope in relation to micturition apparently had not been described. Characteristic of the recorded cases of micturition syncope, as well as of the two reported here, is that these attacks have occurred in healthy, usually young, adults who have no history of fainting at other times.

In the study of Dermksian and Lamb the overt factor at the time of syncope was most often postural changes or pain. They classified the mechanism precipitating syncope under six general types of disorders: (1) inadequate venous return, (2) inefficient cardiac

pumping action, (3) loss of arteriolar tone, (4) abnormalities in the constituents of the circulating blood, (5) inadequate circulating blood volume, and (6) local disorders of the central nervous system. Perhaps two or more of those factors are present in micturition syncope if the explanation suggested by Proudfit and Forteza[3] is correct. They suggest that the mechanism of micturition syncope is the performance of the Valsalva maneuver at the beginning of urination. They relate the syncope to the fall in blood pressure and the rise in intracranial extravascular pressure that occurs with the maneuver. This results in a decrease in cerebral blood flow and hence fainting. However, since in all 7 of their cases the syncope occurred only when micturition was performed immediately after having been in the recumbent position, they suggest that the peripheral pooling resulting from recumbency may contribute to the mechanism. In five of the six episodes in the two cases reported here, the act of micturition occurred immediately after recumbency. In the one instance when it did not there had been prior alcohol ingestion. It may be postulated that peripheral vasodilatation associated with the alcohol ingestion may have been a contributing factor. The intake of alcohol was not infrequently a factor in the cases of syncope reported by Dermksian and Lamb.

It is interesting that all 7 of Proudfit and Forteza's cases were in men, as were the two reported here. The 4 cases mentioned by Dermksian and Lamb were also in men but no conclusion can be drawn from this as their entire series was from an all male population of military personnel. As Proudfit and Forteza point out, women might not be expected to be subject to this condition because of the anatomy of the female urethra and the position assumed during urination.

Summary

Two cases of micturition syncope are reported. This condition apparently has not until recently been described.

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There are many points of interest in Atlanta—namely, Stone Mountain; the home of Uncle Remus; various relics from the War Between the States; and sites where some of the war took place; Cyclorama painting of the Battle of Atlanta; the High Museum of Art; the educational institutions; State Capitol; Municipal Airport and the Federal Penitentiary.

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Pregnancy in the Latter Years of Reproductive Life*

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Pregnancy in a woman forty years or over is, at best, uncommon, becoming increasingly so as the years advance. Complications of general health, as well as those of pregnancy and labor themselves, may be troublesome and particularly may be lethal to the child. This is a most interesting summary of the problem.

A STUDY OF PREGNANCY in the latter years of reproductive life was initially prompted by the seemingly high incidence of patients aged 40 and over encountered in the senior author's private practice. It was thought that pregnancy in this age group was becoming more frequent due to the increased number of marriages late in life, as well as the tendency toward larger families since World War II. While investigating the incidence of pregnancy in this age group at the Georgia Baptist Hospital in Atlanta, a number of interesting complications were noted and provoked enough interest to make the present study.

A number of excellent papers have appeared concerning the elderly nullipara and the dangerous grand multipara, but relatively few studies have appeared with the aging process under consideration. Davis and Seski[1] reviewed 1,011 women, aged 40 and over, at the Chicago Lying-In Hospital in 1948, their cases dating back to 1927. Stanton,[2] in 1956, collected 160 viable births and 77 early pregnancies in women 44 years of age and over.

The childbearing function commences in the second decade of life and ends in the fifth decade. Throughout life anatomic structures vary with age. Physiologic, as well as metabolic processes, are altered at different periods in the life of the female. Since the aging process manifests itself mainly in the replacement of normal tissue by fibrous tissue, some women age faster than others depending on heredity, environment, previous diseases, nutrition, occupation, habits, previous pregnancies with their associated problems, and other stresses in life. Undoubtedly all these factors play some role in the aging process but are difficult to assess. A very extensive analysis would be necessary to study all the varied aspects of reproduction in the latter years of childbearing. It is not the purpose of this paper to attempt any extensive analysis but to review with a few illustrative tables, the incidence of viable births in women aged 40 and over, the complications of these pregnancies and the methods of delivery. A few comments will be made on interesting associated factors that were found in the charts of these patients.

The problem of abortion occurring in the final years of reproductive life is omitted from this study simply because the hospital admissions for abortions in any age group do not represent the over-all incidence of abortion. Therefore no attempt was made to substantiate the previously reported increased incidence of abortion in the latter years of reproductive life.

Clinical Material

The number of women aged 40 and over reaching the stage of viability (28 weeks) during the 5 year period, July 1, 1953, to June 30, 1958, were investigated at the Georgia Baptist Hospital in Atlanta. There were 232 such patients during this period in which there was a total of 18,037 viable births, an incidence of 1.34 per cent. In this group were 33 nulliparous and 199 multiparous women. Fifteen of the multiparas had had six or

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TABLE 1

AGE DISTRIBUTION

Age	Nullipara No.	Nullipara Per Cent	Multipara No.	Multipara Per Cent	Total No.	Total Per Cent	Hospital Per Cent
40	14	6	78	33.6	92	39.7	
41	7	3	45	19.4	52	22.4	
42	7	3	36	15.5	43	18.5	
43	3	1.3	20	8.6	23	9.9	
44	1	0.4	11	4.7	12	5.2	
45	0	0.0	6	2.6	6	2.6	
46	1	0.4	0	0.0	1	0.4	
47	0	0.0	2	0.9	2	0.9	
48	0	0.0	1	0.4	1	0.4	
Total	33	14.2	199	85.8	232	1.3	18,037 Deliveries

more previous viable births and may be classified as grand multiparas.

The distribution of cases of pregnancy at age 40 and over can be seen in table 1. The correct ages of these patients were cross checked by the attending physician's recorded maternal age on the prenatal record, the husband's statement of his wife's age on the hospital admission record, and the patient's statement of her age on the infant's birth certificate form. Surprisingly in only three of these cases did the given age conflict. The youngest age was chosen for the table.

It is interesting to note how rapidly and proportionately the incidence of viable births decreases as the age increases. After age 45 viable births were few in occurrence. Not any patient in this group was over 48 years of age and this agrees with Eastman's[3] statement that viable births after the age of 48 are exceedingly rare. Stanton,[2] in 1956, inquired at several large maternity centers to determine the incidence of viable births at age 50 and over. In over 300,000 deliveries he found no recorded viable births at age 50 and over, but three births at age 49 were recorded. The United States Bureau of Vital Statistics[4] for 1949 reports the incidence of viable births in women aged 50 and over to be one in 24,000 deliveries but the accuracy of these figures is questioned by many. Very rarely has there been found an authentic case of a viable birth after 50 years. A few case reports of pregnancy after the menopause terminating in abortion have appeared in the literature, the most recent instance being in a 56 year old woman reported by Anderson.[5]

It may be interesting to state at this point that there were 4 patients who appeared in this group on two occasions. An additional 4 patients had hospital admissions for abortions subsequent to a viable birth at age 40 or over.

Complications of Pregnancy

The vascular system probably exhibits the most prominent evidence of aging. However, obesity, fibroids, and diabetes mellitus may likewise be associated with aging.

As seen in table 2 the incidence of *chronic vascular disease* in these women, aged 40 and over, is found to be increased nine times the hospital incidence. The classification of chronic vascular disease in this table is based on the degree of vascular changes at ophthal-

TABLE 2

COMPLICATIONS OF PREGNANCY RELATED TO AGING PROCESS

	Nullipara No.	Nullipara Per Cent	Multipara No.	Multipara Per Cent	Total No.	Total Per Cent	Hospital Incidence Per Cent
Chronic vascular disease	12	5.2	52	22.4	64	27.6	3.2
Mild	10	4.3	39	16.4	49	20.7	2.5
Moderate	2	0.9	11	4.7	13	5.6	0.6
Severe	0	0.0	2	0.9	2	0.9	0.1
Diabetes mellitus	0	0.0	2	0.9	2	0.9	0.1
Fibromyoma	2	0.9	9	3.9	11	4.7	0.1
Obesity	12	5.2	58	25.0	70	30.2	8.

moscopic examination, as well as blood pressure recordings at the initial prenatal visit. These examinations, as far as possible, were correlated with the findings at the time of delivery. In one of the two severe cases of chronic vascular disease a cerebral thrombosis with a right hemiplegia occurred at 14 weeks gestation with almost complete recovery when she delivered near term.

Obesity is a frequent finding in this age group and often predisposes to hypertension and chronic vascular disease. The incidence of women beginning their pregnancy weighing 150 pounds or more is found to be 30.2% compared to the average hospital incidence of 8% for women with an average height of 64.2 inches. A survey of statistics compiled by the Metropolitan Life Insurance Company reveals that 23.8% of women between the ages of 40 and 50 years are 20% or more over the normal weight for their average height.

Diabetes mellitus is an inherited metabolic disease which may be found in any age group, but is detected clinically with greater frequency in middle age than at any other time. This disease is often associated with obesity and enhances the development of chronic vascular disease. The number of cases found in our present study is not great but represents an increased incidence some seven times the hospital incidence.

Fibromyoma uteri is also an expected finding associated with aging. These tumors are most frequently found in the latter years of reproductive life. The number of cases was expected to reach an incidence nearer 10% rather than an incidence of 4.8 per cent. However, these tumors apparently play some role in fertility in this age group. Most of the tumors were detected at the initial prenatal visit. One, however, was a pathologic as well as clinical diagnosis and served as the indication for one of the cesarean hysterectomies performed. Two patients had findings consistent with degenerating processes involving the fibroids during their pregnancies.

The *multiple complications* encountered in reviewing the histories and prenatal records of these patients can be seen in table 3. These complications are not necessarily associated with aging but are diversified and interesting from this standpoint. No attempt was made to compare them with the hospital incidence because of this diversity. It seems that anemia would not be a problem but 8 or 3.5% had hemoglobin determinations of less than 10 Gm. during their pregnancy or at the time of admission to the hospital in labor. The two cardiac patients were known to have had rheumatic heart disease for several years. The pulmonary complications included 3 patients who had chronic asthma with varying degrees of emphysema. There were two cases of tuberculosis in the series; one of the patients had active disease as detected at the initial prenatal visit by chest x-ray film. The other tuberculous patient had arrested disease but had a hip joint deformity with ankylosis resulting from an old tuberculous osteoarthritis. In addition, one patient had marked kyphoscoliosis with limited thoracic mobility resulting in a very low vital capacity. The surgical complications included one instance of acute appendicitis with operation at 18 weeks gestation. A carcinoma of the breast in the twenty-eighth week of gestation was detected at a routine prenatal visit. A radical mastectomy was per-

TABLE 3

COMPLICATIONS OF PREGNANCY NOT RELATED TO AGING

	Nullipara		*Multipara*		*Total*	
	No.	*Per Cent*	*No.*	*Per Cent*	*No.*	*Per Cent*
Anemia	1	0.4	7	3.	8	3.5
Heart disease	1	0.4	1	0.4	2	0.9
Pulmonary complications	2	0.9	5	2.2	7	3.
Appendicitis	0	0.0	1	0.4	1	0.4
Cancer breast	0	0.0	1	0.4	1	0.4
Dermatitis	0	0.0	2	0.9	2	0.9
Nervous system	1	0.4	3	1.3	4	1.7
Diastasis recti	0	0.0	2	0.9	2	0.9
Varicosities	0	0.0	10	4.3	10	4.3
Renal complications	1	0.4	6	2.6	7	3.

TABLE 4

TOXEMIA OF PREGNANCY

	Nullipara		*Multipara*		*Total*		*Hospital*
	No.	*Per Cent*	*No.*	*Per Cent*	*No.*	*Per Cent*	*Per Cent*
Toxemia pregnancy	8	3.5	10	4.3	18	7.8	2.2
Mild	4	1.7	7	3.	11	4.7	1.6
Pre-eclampsia	4	1.7	2	0.9	6	2.6	0.4
Eclampsia	0	0.0	1	0.4	1	0.4	0.1
Superimposed toxemia	3	1.3	7	3.	10	4.3	0.5

formed at 29 weeks gestation with no metastatic involvement of the axillary nodes found on pathologic examination. This patient subsequently had a normal delivery and has shown no evidence of metastases over a period of 2 years following the radical operation. Oddly enough, 2 patients with erythema multiforme were encountered on admission in labor. Many of the patients exhibited some degree of emotional instability during their pregnancy. Two patients had major psychotic episodes during pregnancy with one having to receive electroshock therapy in the second trimester of pregnancy. Other complications of the nervous system included one victim of an automobile accident who sustained a cerebral concussion and remained unconscious for 4 days at a gestational stage of 26 weeks. The other patient had total maternal blindness. Two multiparas exhibited a pronounced diastasis recti with pendulous abdomens requiring support. Varicosities were prominent in 4.3% of the group, two of whom had extremely large vulval varicosities. One of the patients with vulval varicosity had a hemorrhage from it near term while taking a bath and required blood replacement. The renal complications included two patients with bilateral nephrolithiasis and chronic pyelonephritis. One case of interstitial cystitis was encountered. The remaining renal complications were due to acute pyelitis of pregnancy.

It is probably true that some of these complications are more the result of multiparity than aging, especially diastasis recti and varicosities. Several of these complications were noted to be the indication for postpartum sterilization, especially varicosities.

Toxemia of pregnancy is a condition peculiar to childbearing. However, aging with its associated vascular and metabolic changes probably contributes to an increased incidence. As seen in table 4, toxemia is found to be three and one-half times the hospital incidence. This compares favorably with the Davis and Seski[1] study made in 1948. There was but one eclamptic in our group of patients, but four of the multiparas gave a history of eclampsia with a previous pregnancy. In the one case of eclampsia the patient showed no toxic symptoms during her pregnancy, but on admission to the hospital in labor her blood pressure was elevated and she had albuminuria. After a rather rapid labor she had one convulsive seizure in the immediate postpartum period. The classification of mild toxemia in this table pertained to patients who had an elevation of blood pressure near term associated with edema and rapid weight gain, but had not reached the degree of severity to cause albuminuria. The incidence of superimposed toxemia rather closely parallels the incidence of chronic vascular disease. Most of the patients with su-

TABLE 5

LABOR

	Nullipara		*Multipara*		*Total*		*Hospital*
	No.	*Per Cent*	*No.*	*Per Cent*	*No.*	*Per Cent*	*Per Cent*
Prolonged—25 hrs. or more	3	1.3	1	0.4	4	1.7	0.2
Precipitate—3 hrs. or less	1	0.4	28	12.1	29	12.5	8.8
Inertia	5	2.2	7	3.	12	5.2	3.2
Primary	3	1.3	4	1.7	7	3.	1.6
Secondary	2	0.9	3	1.3	5	2.2	1.6
Induction labor	1	0.4	18	7.8	19	8.2	6.9

TABLE 6

PRESENTATIONS AND POSITIONS

	Nullipara		Multipara		Total		Hospital
	No.	Per Cent	No.	Per Cent	No.	Per Cent	Per Cent
Occiput anterior	26	11.2	175	75.4	201	86.6	90.04
Persistent occiput posterior	3	1.3	10	4.3	13	5.6	3.1
Occiput transverse	1	0.4	2	0.9	3	1.3	1.8
Breech	2	0.9	7	3.	9	3.9	3.9
Compound	1	0.4	1	0.4	2	0.9	0.1
Face	0	0.0	1	0.4	1	0.4	0.1
Transverse	0	0.0	2	0.9	2	0.9	0.1
Twins	0	0.0	1	0.4	1	0.4	11.

perimposed toxemia had a rising blood pressure with edema as they neared term.

Complications of Labor

The labor records of these cases were reviewed with the hope of finding many interesting complications. The incidence of prolonged labor was increased seven times the hospital incidence. The incidence of precipitate labor, or labor 3 hours or less in duration, as well as uterine inertia was between one and one-half to two times the hospital incidence as we see in table 5. Labor was induced in 8.2% of these patients as compared to the hospital incidence of 6.9 per cent. One-half of the indications for induction of labor in these patients included multiparas classified as nonresidents who had given a history of previous rapid labor. Most of the other inductions were performed because of toxemia.

The presentations and positions are tabulated in table 6, and we find no significant variation as compared to the over-all hospital incidence.

The methods of delivery may be seen in table 7. The incidence of cesarean section is only two times greater than the hospital incidence. It should be noted that the number of subsequent operations in this group is 40% as compared to the hospital rate of 45% for subsequent cesarean sections. One patient scheduled for a second cesarean section had a precipitous labor and delivery while in the hospital the night prior to the anticipated operation the following morning. Two cesarean hysterectomies were performed and are included in the sterilization procedures. One of these previously mentioned was done because of fibromyoma at age forty-seven. The other was performed as a second cesarean section because the old uterine scar had begun to separate in a patient aged forty-three. The forcep deliveries in this group is slightly less than the over-all hospital incidence with the exception of midforceps, which is almost two times the hospital rate. One of the two versions and extractions was performed for a known abnormally developed infant presenting obliquely. The other was done in a multipara who was almost completely dilated with membranes intact on admission to the hospital and with a shoulder presentation. There was a total of 14 postpartum tubal ligations. Five postpartum tubal ligations were performed in patients aged forty. There were also 5 in the 41 year old group, 3 in the 42 year group, and one at age forty-three.

TABLE 7

TYPES OF DELIVERIES

	Nullipara		Multipara		Total		Hospital
	No.	Per Cent	No.	Per Cent	No.	Per Cent	Per Cent
Spontaneous	18	7.8	165	71.1	183	78.9	77.8
Cesarean section	3	1.3	7	3.	10	4.3	2.1
Cesarean hysterectomy	0	0.0	2	0.9	2	0.9	
Repeat	0	0.0	4	1.7	4	1.7	45.
Forceps	12	5.2	25	10.8	37	16.	19.9
Low	7	3.0	21	9.1	28	12.1	17.9
Mid	5	2.2	4	1.7	9	3.9	2.1
Version and extraction	0	0.0	2	0.9	2	0.9	0.2
Postpartum sterilization	0	0.0	16	7.	16	7.	1.7

TABLE 8

FETAL OUTCOME
WOMEN 40 AND OVER (252 CASES)

	Nullipara		Multipara		Total		Hospital
	No.	Per Cent	No.	Per Cent	No.	Per Cent	Per Cent
Viable births	53	14.2	199	85.8	252	1.34	18,037 Deliveries
Maternal mortality	0	0.0	0	0.0	0	0.0	.005
Perinatal mortality	7	3.	10	4.3	17	7.3	2.6
Stillborn	5	2.2	6	2.6	11	4.7	1.2
Neonatal deaths	2	0.9	4	1.7	6	2.6	1.5
Fetal anomalies	1	0.4	5	2.2	6	2.6	1.0
Premature births	9	3.9	14	6.	23	10.0	5.8

The increased incidence of postpartum sterilization procedures was an expected finding but there is some doubt in our minds if this figure, some four times greater than the hospital incidence, is justified, since the probability of another pregnancy in the final stages of reproductive life becomes progressively lessened.

The outcome of these pregnancies reaching the stage of viability was found to be quite interesting and may be seen in table 8. Fortunately there was no maternal mortality. The perinatal mortality was three times the hospital incidence and was proportionately higher for the group of nulliparas. Uncontrolled maternal diabetes mellitus and a severe RH incompatibility each accounted for one of the stillbirths in the multiparous group. There were two congenital anomalies incompatible with life. The remaining instances of stillbirths were due to either abruptio placenta or severe toxemia. The neonatal deaths consisted mainly of premature infants. One neonatal death occurred in a child with a major congenital deformity.

The incidence of fetal anomalies was found to be two and one-half times the hospital incidence. These anomalies included three mongoloid infants. Fortunately, a very close follow-up for mongolism was obtained through the efforts of one of the pediatricians who was making a simultaneous study of mongoloid infants born at the Georgia Baptist Hospital. One of the mothers who delivered a mongoloid infant gave a history of a previous birth at age 37 of a mongoloid infant. Penrose,[6] in England, found that 40% of mongoloid children were born to mothers aged 40 and over. The remaining congenital anomalies consisted of one cranial monstrosity incompatible with life with an associated meningocele, one stillborn having an interventricular septal defect and one neonatal death of an infant with a congenital fissure of the skull and spinal column.

Penrose[6] is of the opinion that the environmental factors dependent on the maternal conditions are important as predisposing causes of fetal anomalies in the latter years of reproductive life. These same environmental factors may be operative in the causation of an increased number of premature infants according to weights, since 9 of the premature infants born had reached at least 38 weeks gestational age. There were 10 early spontaneous labors resulting in premature births and 4 induced premature births. In the 9 instances where 38 weeks gestational age had been reached, the fetal environment may be implicated since 8 of these infants were born to mothers with either moderate or severe chronic vascular disease and the other occurred in a fibromyomatous uterus. If these 9 instances of premature infants were the result of maternal conditions and were excluded, then the incidence of premature births

TABLE 9

HEMORRHAGES OF PREGNANCY

	Nullipara		Multipara		Total		Hospital
	No.	Per Cent	No.	Per Cent	No.	Per Cent	Per Cent
Placenta previa	1	0.4	2	0.9	3	1.3	0.5
Marginal sinus	1	0.4	5	2.2	6	2.6	2.2
Abruptio placenta	2	0.9	1	0.4	3	1.3	0.4
Postpartum hemorrhage	2	0.9	7	3.	9	3.9	2.5

would be almost identical with the hospital incidence.

The hemorrhagic complications of pregnancy and the puerperium may be seen in table 9. The incidences of placenta previa and abruptio placenta were both increased approximately three times the hospital incidence, while ruptured marginal sinus compared more closely to the hospital incidence. Postpartum hemorrhage on the other hand was almost two times the expected incidence. There was one delayed postpartum hemorrhage which occurred on the eighth postpartum day. Manual exploration of the uterus at the end of the third stage of labor was performed in 18% of these cases. Hematoma of the vulva occurred in 3 patients, all multiparas. One was associated with vulval varicosities, another with a prolonged second stage of labor and the third occurred in a difficult midforcep delivery.

The postpartum period was found to be relatively uncomplicated with the exception of the previously mentioned conditions. There were few instances of maternal morbidity. Urinary retention was a problem in four nulliparas and one multipara. The remaining instances of maternal morbidity resulted mainly from mild endometritis or mastitis.

Interval Since Last Preceding Pregnancy

Because of the anxiety exhibited by many patients at this age of possibly being pregnant and the surprise that some registered after learning they were pregnant after varying intervals of marriage or since the birth of their last child, it was decided to investigate this interesting aspect of reproduction in this group of patients.

In the multiparous group of patients as seen in table 10 it was found that 66.8% had had a viable birth less than 10 years prior to the present birth. There was a total of 47 patients or 23.6% who had an interval of 10 to 15 years since their last viable birth. Fifteen or 7.5% had had an interval of 15 to 20 years since their last viable birth. Four or 2% had had an interval of 20 years or more between viable births. In the last three groups 5 patients had been divorced and remarried with an interval of 10 years or longer between births.

TABLE 10

INTERVAL BETWEEN PREGNANCIES (MULTIPARA)

Years	*No.*	*Per Cent*
Less than 10	133	66.8
10	47	23.6
15	15	7.5
20	4	2.

TABLE 11

INTERVAL BETWEEN MARRIAGE AND PREGNANCY (NULLIPARA)

Years	*No.*	*Per Cent*
Less than 10	19	57.6
10	2	6.1
15	8	24.2
20	4	12.1

In the nulliparous group of patients, 19 or 57.6% had been married either for the first time or with a subsequent remarriage less than 10 years when they first gave birth to a viable infant. Only two or 6.1% of the nulliparas had been married between 10 and 15 years. However, 8 or 24.3% of this group had been married between 15 and 20 years when their infant was born, and 4 or 12.1% had been married 20 or more years before carrying a pregnancy to a viable period of gestation. One woman in this last group had been married twice and yet the interval of her second marriage was still 20 years before she delivered a normal infant at age forty-two (Table 11).

Summary

A brief review of the literature concerning pregnancy in the latter years of reproduction is presented. Two hundred and thirty-two cases of viable births in women aged 40 and over were reviewed at the Georgia Baptist Hospital in Atlanta.

The age distribution of viable births in these patients, age 40 and over, are presented. The complications considered more closely associated with aging such as chronic vascular disease, obesity, diabetes, and fibromyoma uteri are discussed and compared with the hospital incidence. The multiple diversified complications not necessarily associated with aging are tabulated and briefly discussed. Toxemia of pregnancy, complications of labor, and methods of delivery, as well as sterilization procedures, were investigated and results presented. Analysis of the outcome of these pregnancies reaching the stage of vi-

ability included maternal mortality, perinatal mortality, fetal anomalies, and premature births. The hemorrhages of pregnancy are likewise presented. An interesting analysis concerning the interval between marriage and viable birth in the nulliparous group and the interval between viable births in the multiparous group was made.

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Discussion (Abstract)

Dr. Seward H. Wills, Houston, Tex. Dr. Calk has presented a most interesting and worthwhile report on pregnancy in women 40 years or more of age. This represents an excellent study of these patients and is of value to us as practicing physicians in answering the question so often asked, "Am I too old to have a baby?"

Dr. Calk's incident of pregnancy of 1.4% in women 40 years or more is comparable to that of Davis and Seski of 1.8% and both show a rapid drop after 46 years of age. Stanton reported on women over 44 years a rate of 0.2 per cent.

As we might suspect, the most frequent complication was of the vascular system. In Dr. Calk's series the incident of vascular disease was 9 to 10 times that of the hospital incident; however, that of the Davis series was only 3 times the hospital incidence.

I think the finding of the number of cases of obesity of 30.2% compared to the hospital incidence of 8% is a significant point and an expected one, considering the metabolic change accompanying aging, as is the incidence of diabetes of 7 times the hospital incidence.

The incidence of toxemia being about three and a half times greater than the average compares with the Davis and Stanton reports and is the greatest cause of increase in operative deliveries and fetal loss.

Dr. Calk's rate of cesarean sections was twice normal, which makes me believe the Atlanta obstetricians are conservative. The Davis section rate was three times greater. The prolonged labors were seven times the average with twice the number of midforceps deliveries, which allows one to speculate if the section rate should not have been a little higher.

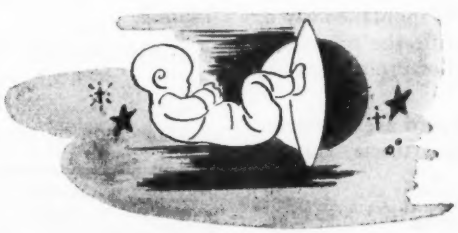
The perinatal rate was three times the hospital rate which compares favorably with Davis' who states that one out of every 10 women failed to take a baby home with her. The high mortality was occasioned by prematurity resulting from severe toxemia and the high rate of hemorrhage in the third trimester.

The incidence of fetal anomalies was found to be two and a half times the hospital incidence and these included three mongoloid infants which is comparable with the Davis series.

The increase in vascular diseases, obesity, toxemias, prematurity and congenital deformities are all factors to be considered in the evaluation and treatment of women over 40 years of age.

Dr. Calk believes that his sterilization rate of four times the normal incidents is high. I feel that physicians who do not want these patients to become pregnant should sterilize them, since there still is the possibility that they will become pregnant as is shown by the fact that there were 4 patients who appeared in this group on two occasions.

This study helps confirm the prevalent opinion of the increased risks to mother and baby in women of 40 years or more and confirms previous reports. We are indebted to Dr. Calk for this excellent report.



Prolapse of the Umbilical Cord:

An Analysis of 123 Cases*

WILLIAM H. ROBERTSON, M.D.,† *Birmingham, Ala.*

Fetal mortality is high if prolapse of the cord occurs. The predisposing causes are considered, and induction of labor seems to be important among these. Methods of prevention and treatment have been outlined.

PROLAPSE OF THE UMBILICAL CORD is an obstetric complication which causes fetal anoxia and often fetal death. The purpose of this paper is to present the experience with this complication on the indigent service of the University Hospital during the 9 year period from January 1, 1949, through January 31, 1958.

Incidence

The incidence has been reported as high as one in 74 deliveries by Cragin[1] and as low as one in 1,018 deliveries by Doerr.[2] Slate and Randall[3] reviewed the statistics of 24 authors and found the average incidence to be one in 156 deliveries. In the present series there were 123 occurrences of prolapsed cord in 28,988 deliveries or one in 235 deliveries (Table 1).

TABLE 1

Charity Hospital of New Orleans	1:499	(0.22%)
State University of Iowa Hospital	1:250	(0.40%)
University Hospital	1:235	(0.42%)

Etiology

There are many factors which are etiologically important in prolapse of the cord. Any condition which causes maladaptation of the presenting part to the true pelvis can predispose to prolapse of the umbilical cord. This includes cephalopelvic disproportion, abnormal presentations, obstructed birth canal, prematurity, multiple pregnancy, fetal deformities and polyhydramnios. Abnormally long cords are thought to prolapse more frequently than short ones.

If the membranes rupture spontaneously or are ruptured artificially while the presenting part is high, the likelihood of prolapse of the cord is great.

Many cases of prolapsed cord are iatrogenic since they are produced by artificial rupture of the membranes to induce or stimulate labor. It is the practice of some to push the presenting part up at the time of amniotomy to allow more amniotic fluid to drain off. While no one doubts the value of this procedure in terms of facilitating uterine contractions, the incidence of prolapsed cord in such cases is greatly increased. The use of other obstetric manipulations, such as insertion of the Voorhees' bag, catheters and packs, may lead to dislodgment of the presenting part, rupture of the membranes and prolapse of the cord. Indeed, even rectal and vaginal examinations during labor can cause dislodgment of the presenting part and rupture of the membranes. It is possible that over-distention of the bladder could lead to disengagement of the presenting part.

In this series, elective amniotomy was performed 26 times for induction or stimulation of labor. It was felt that all inductions were for valid obstetric indications. The Voorhees' bag was used 3 times for induction of labor.

The percentages of occurrences of the various presentations in our cases are given in table 2.

It may be seen that the majority of cases

TABLE 2

PERCENTAGE OF DIFFERENT PRESENTATIONS IN CASES OF PROLAPSED CORD

Author	*No. Cases*	*Vertex*	*Breech*	*Transverse*
Kush[4]	105	52.0	29.0	19.0
Slate and Randall[3]	59	58.0	22.0	12.0
Robertson	113	51.3	38.9	9.7

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FIG. 1

COMPARISON OF PARITY TO INCIDENCE OF PROLAPSED CORD

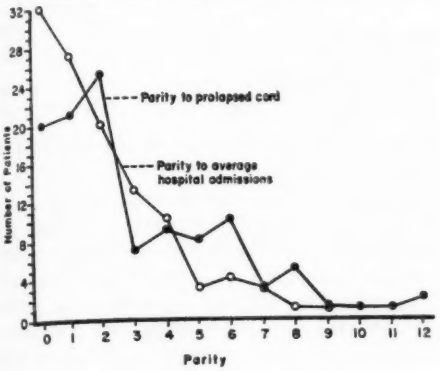
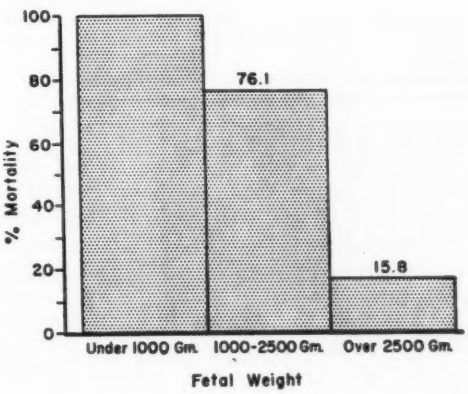


FIG. 2

RELATION OF FETAL WEIGHT TO FETAL MORTALITY



occur in vertex presentations. The occurrence in breech and transverse presentations is seen to be disproportionately high when one realizes that the usual incidence of breech deliveries is about 3% and that of transverse 0.5 per cent.

It has been said that multiparas are more prone to develop prolapsed cord because the lower uterine segment is less closely adapted to the presenting part. In this series there were 20 primigravidas and 94 multigravidas. This was an occurrence rate of 17% in primigravidas which can be compared with an incidence of 29% primigravida admissions. The relationship is shown in figure 1.

Fetal Mortality*

The most important consideration in cases of prolapsed cord is fetal salvage. The over-all fetal mortality in this study is 35 per cent. Forty babies were lost. When this is corrected to include infants weighing over 1,000 Gm. the fetal mortality rate is 25 per cent. Analysis of 12 different series revealed a gross fetal mortality ranging from 11.4 to 63 per cent. Figure 2 and table 3 show the fetal mortality in the three weight groups.

Fetal mortality may be analyzed in various ways. Fetal presentation is an important consideration. Table 4 gives the results in the various presentations in our series of cases.

In general it would appear that the fetal salvage is better when the position is breech or transverse. This would seem logical when one considers the relative inelasticity of the fetal skull. The low incidence of fetal mortality in transverse presentations differs from that reported by most authors.[5-7]

Fetal salvage and the degree of cervical dilatation is analyzed in table 5.

The more nearly complete the cervical dilatation when the prolapse occurred the better the fetal prognosis. The time element is, of course, the important factor. The sooner the delivery can take place the better the fetal outlook.

As could be expected, the fetal salvage was much better when the membranes ruptured in the hospital. There were 37 cases where the membranes ruptured at home. The fetal mortality was 60% or 14 babies lost in 23 deliveries. All of these weighed over 1,000 Gm. There were 77 cases in which the membranes ruptured in the hospital and of these, 15 babies or 19% were lost.

Antepartum Care

It is believed that antepartum care is im-

TABLE 3

FETAL MORTALITY

Cases	*Under 1,000 Gm.*	*1,000 to 2,500 Gm.*	*2,500 Gm. and Over*
11	11		
21		16	
82			13

*In some instances the chart did not provide sufficient information as regards fetal weight, salvage, etc. In other instances the charts were lost. This explains apparent discrepancies between percentages and total number of cases. Percentages were corrected so as to include only cases where sufficient information was available.

TABLE 4

FETAL MORTALITY AND PRESENTATION

Presentation	Incidence	Under 1,000 Gm.	1,000 to 2,500 Gm.	2,500 Gm. and Over
Vertex	58(51.3%)	2	6	14
Breech	44(38.9%)	9	7	1
Transverse	11(9.7%)	0	0	1

portant in a series of this sort. It is logical to assume that patients who have received medical care during their pregnancy would be more likely to seek early medical advice when the membranes rupture or when labor begins. In the present series 92 patients had antepartum care, and in this group the fetal results were good in 65 and poor in 27. Twenty patients had no antepartum care and the fetal results were good in 7 and in 13 poor (Table 6).

Treatment

The definitive treatment for prolapsed cord is delivery as soon as possible if the baby is alive (Figs. 3 and 4). Intelligent urgency should be the keynote of the therapeutic regimen. Panic should be avoided. Supportive therapy designed to relieve pressure on the cord and to increase fetal oxygen saturation should be instituted at once. These measures include the knee chest position if the cord is posterior to the presenting part, the deep Trendelenburg position if anterior to the presenting part, and manual displacement of the presenting part off of the cord with maintenance of this station. Oxygen should be administered to the mother simultaneously. It is felt that attempts to replace the cord and the use of cord protectors waste valuable time. This inference is personal and cannot be concluded from the study since intelligent and careful attempts to replace the cord were not tried. The Voorhees' bag would also fall into this category. In this study the bag was used 4 times as treatment; 2 of these babies were lost.

The choice of type of delivery involves

TABLE 5

CERVICAL DILATATION AND FETAL MORTALITY

Cervical Dilatation	No. Cases	1,000-2,500 Gm.	2,500 Gm.
0-5 cm.	26	8	6
6-7 cm.	18	3	1
8 to complete	42	2	3

TABLE 6

		Fetal Results Good	Poor
With Antepartum Care Number of Patients	92	65	27
Without Antepartum Care Number of Patients	20	7	13

many factors. A summary of the methods of delivery is given in table 7.

In general, those cases most nearly ready for delivery should show the best fetal salvage. In the spontaneous delivery group were 5 women admitted with prolapsed cord without pulsation. Of the 5 women in whom breech extractions were done with a stillborn baby, 4 were admitted with a prolapsed cord without pulsations. One of the version and extractions was done in a case in which a transverse presentation was present and in whom no fetal heart tones had been heard.

Since version and extraction has become a controversial procedure further evaluation is indicated. Of 28 versions and extractions done 6 babies were lost. Four were stillborn and 2 died in the neonatal period. One of the 4 stillbirths was a baby who had died in the intrapartum period. Five babies were lost, possibly as a result of the version and extraction. All of these babies weighed over 1,000 Gm.

Other complications associated with the version and extraction were:

Cervical laceration	4
Puerperal endometritis with morbidity	1
Postpartum hemorrhage	2
Uterine laceration (incomplete)	1

The uterine laceration was an extention

FIG. 3

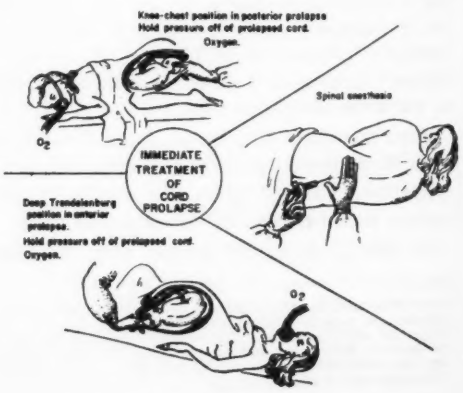
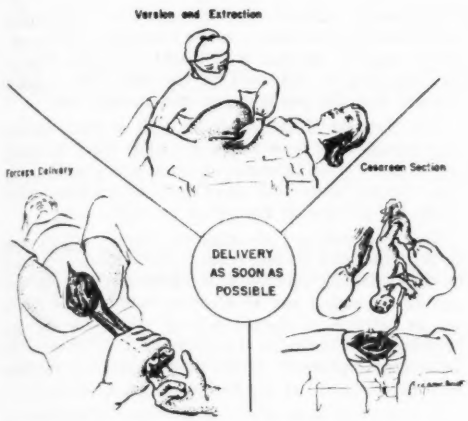

Knee-chest position in posterior prolapse
Hold pressure off of prolapsed cord.
Oxygen.
Spinal anesthesia
IMMEDIATE TREATMENT OF CORD PROLAPSE
Deep Trendelenburg position in anterior prolapse.
Hold pressure off of prolapsed cord.
Oxygen.

FIG. 4



into the lower uterine segment from a cervical tear and was repaired from below. This patient had an uncomplicated postpartum course and since then has been delivered successfully from below. When one realizes that the cases in which treatment was by version and extraction would not meet the criteria for early spontaneous or low forceps delivery the results are good.

The most important considerations when deciding the treatment of choice are cervical dilatation, pelvic adequacy, station of the presenting part, and viability of the fetus. If conditions are favorable for immediate vaginal delivery, either spontaneously or with the help of forceps, this should be done. The position of the version and extraction procedure in the therapeutic regimen depends also on the cervical dilatation, pelvic adequacy, and the skill of the operator. This study was not undertaken to prove the value of the version and extraction, but to report our experiences. If all of the criteria are not met it is believed that cesarean section is the method of choice. A spinal anesthesia can be given immediately while preparations are being made for the section. This will facilitate the attempts to keep the presenting part from compressing the cord.

TABLE 7

TYPE OF DELIVERY AND FETAL MORTALITY

Type of Delivery	*No. Deliveries*	*Stillborn Over 1,000 Gm.*	*Neonatal Death Over 1,000 Gm.*
Spontaneous	30	13	2
Forceps (low)	12	1	0
Forceps (mid)	2	0	0
Version and extraction	28	4	2
Cesarean section	3	0	0
Breech extraction	39	5	2

Prevention

It is believed that the increasing popularity of elective inductions and "babies by appointment" may lead to an increased incidence of prolapse of the umbilical cord (Fig. 5). While no one denies the effectiveness of amniotomy in induction of labor, the dictum of Osler to "do no harm" should be heeded. One should be certain that there is adequate engagement before performing the amniotomy. It is thought that the practice of pushing up the presenting part to drain out more fluid is hazardous. Other methods of induction such as use of the Voorhees' bag, catheters and packs should be viewed with caution. Rupture of the membranes in situations likely to be complicated by prolapse of the cord should be carefully avoided. These include cephalopelvic disproportion, multiple pregnancy, malpresentation, and polyhydramnios.

Diagnosis

Early diagnosis is extremely important (Fig. 6). There was a delay in diagnosis of the prolapse in 18 of our cases where the membranes ruptured in the hospital. When the membranes rupture the fetal heart tones should be checked immediately and at frequent intervals thereafter. A rectal examination should be done immediately; if there is any question, or if the presenting part is unengaged a vaginal examination should be done. The fetal

FIG. 5

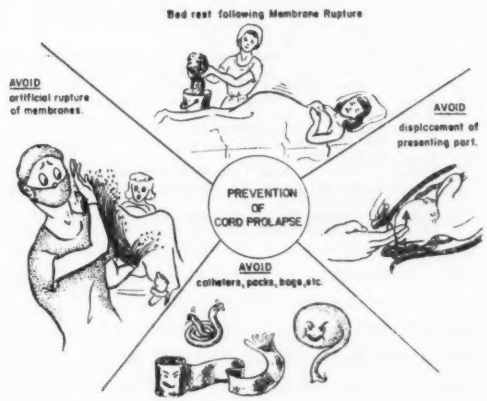
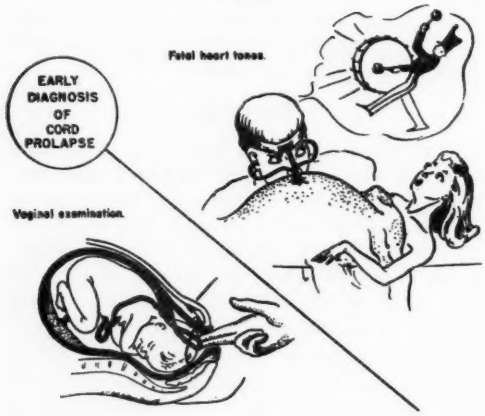


FIG. 6



heart tones should be checked after each rectal or vaginal examination.

Summary and Conclusions

This has been a study of the cases of prolapse of the cord for a 9 year period on an indigent service. The etiology, incidence, and fetal salvage have been discussed. Methods of diagnosis and prevention were mentioned.

It is believed that the incidence of prolapse of the cord may increase with the increase in elective inductions. Fetal mortality remains high in this complication. Awareness of the danger of prolapse of the cord could well reduce the fetal mortality in this condition.

Acknowledgment

I am indebted to Dr. W. N. Jones, Mrs. Jewell Thurman, Mrs. Alice Baggett, and Dr. Gilder Wideman for valuable assistance.

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Discussion (Abstract)

Dr. Haynes Jackson, Hot Springs, Ark. It is readily apparent that the easiest case of prolapse of the umbilical cord to manage is that one in which there is no pulsation of the cord at the time of diagnosis. Beyond that the problem becomes complicated.

The purpose of this study, as well as many similar ones which have been made in recent years, is to see if we can derive information that will enable us to cope better with this condition, and consequently lower the atrociously high fetal mortality rate.

The incidence and the etiologic factors contributing to this condition do not require comment, except that I wholeheartedly agree with Dr. Robertson that in this age of increasing use of elective induction of labor, we as physicians, should adhere closely to the acknowledged criteria for this procedure. Otherwise, the incidence of prolapse of the cord is going to increase as a direct result of our unintelligent meddling.

I would like to comment briefly on the methods of treatment utilized in this particular study.

First, it would seem, in comparison with other studies, that the incidence of spontaneous delivery (approximate 25%) is too high in this series. There were 15 babies, of more than 1,000 Gm. that were lost in this group. Five of these showed no pulsation of the cord on admission. Perhaps a more active plan of treatment could have salvaged some of the remaining 10 babies that were lost.

Second, the incidence of version and extraction is definitely higher in this study than in any comparable series. However, as Dr. Robertson has shown, the results obtained with this method of treatment were good and the complications were minimum. This indicates that the procedure was being done by those who were particularly adept in its use. I believe that most of us would find other methods of treatment to be safer in our hands and that we probably could achieve comparable results.

Third, the incidence of cesarean section in this study is very low, with only 3 sections having been done. A review of the literature reveals that in the series in which there is a greater use of cesarean section the fetal mortality rate is lower.

An analysis of this problem is now being made at the University of Arkansas School of Medicine by Robert Jenkins, a senior medical student, as a part of his senior thesis. This work is incomplete but his data shows 83 cases of prolapse of the cord during the period of 1950 to July, 1958, a comparable incidence to this study. The gross fetal mortality is comparable; however, the breakdown as to salvageable and unsalvageable babies is incomplete. The final figures will be interesting because in these 83 cases there were 20 cesarean sections and only one version and extraction.

I want to thank Dr. Robertson for the privilege of commenting on his paper.

Evaluation of Radiation Therapy of Bladder Carcinoma*

CECIL M. CRIGLER, M.D., GILBERT FLETCHER, M.D., LOWELL MILLER, M.D., and SID JONES, M.D.,† *Houston, Tex.*

The authors evaluate the careful and studied use of a combination of radical irradiation and surgery in the management of malignancy of the bladder.

MY PERSONAL EXPERIENCE of 25 years in urology has afforded sufficient time for appraisal of every possible method of control of bladder cancer. Although review of the extensive literature shows encouraging research data, clinical evaluations, and some surgical triumphs, the paucity of clinical cures is indeed a melancholy subject.

The status of bladder cancer can best be evaluated by study of data in large cancer hospitals or centers. In such centers every stage of bladder cancer can be assessed, as well as the pitfalls that exist in attempts at control. The evidence reported in this survey from a cancer center will include large numbers of cases, data pertinent to meticulous pathologic classification, painstaking clinical evaluations, details referable to surgical procedures, follow-up studies, and finally, calculation of survival data that are definitive as well as dependable.

Over the years, the many methods of treatment devised have been impressive. These include a series of technics, from the early Coffey procedures to the more recent ileal segment diversions, with concomitant simple or radical cystectomies, and in some instances, even complete pelvic exenterations. The number of 5 year survivals achieved by any of these procedures, however, leaves much to be desired. One of the outstanding achievements has been the establishment by Jewett and Strong[1] of a classification that is universally acceptable for grading and staging. With this classification as a true base line for determining the degree and extent of penetration of the bladder wall, as well as the histologic classification of the tumor, the operative prognosis has been sustained even in large heterogenous groups of patients when many different curative procedures have been used.

Low-grade superficial tumors of the bladder do not constitute the most serious problem for the therapist, as management and control by surgical procedures have had comparative success. The penetrating lesions of the infiltrative type are the most difficult and dangerous, and for cure of such tumors all therapeutic modalities have been inadequate.

Because of consistent defeat in efforts to control cancer of the bladder a different approach to the problem was obviously indicated. A closely integrated combination of radiotherapeutic and clinical urologic procedures seemed a possible starting point, with the concepts of Jewett and Strong,[1] as supported by Marshall and Whitmore,[2] as bases for assessment and classification. Whether patients are treated surgically or by irradiation in any of its forms, evaluation and classification methods must be similar for the results to be comparable. Full cooperation between the urologist and radiotherapist is essential for an informative series with accurate interpretation of the results.

Etiology

At this point it is well to consider some of the factors that have been suggested as possible etiologic agents or influences in the development of cancer of the urinary bladder. Seemingly, the incidence is increasing. Dr. D. M. Wallace,[3] of London, stated in a recent Hunterian Lecture that this apparent increase is not necessarily an outcome of improved diagnostic technics. Instead, he suggested that

*Read before the Section on Urology, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

†From the Departments of Urology and Radiotherapy, The University of Texas and the M. D. Anderson Hospital and Tumor Institute, Houston, Tex.

environmental or occupational factors might be contributory, or altered social conditions and personal habits might be significant to this increase. Both clinical experimental evidence and clinical biochemical evidence are available for study. In the former category the possibly carcinogenic effects of urine have been considered as well as the chemical factors in the production of bladder lesions. In experimental animals, if the ureters are transplanted before administration of a carcinogenic diet, the animal does not develop tumor. Therefore, it seemed likely that contact of the urine and the mucosa was necessary to tumor induction. In studies by McDonald and Lund[4] experimental confirmation of urogenic cancer was presented. In the induction of bladder cancer by beta-naphthylamine in experimental animals, the bladder was divided into two compartments by use of a Pavlov pouch technic, each part having an intact blood and nerve supply. The investigators found that carcinoma did not develop in bladder epithelium that was not in contact with urine.

In 1947, Goldblatt reported three factors common to the chemical compounds used in the dye industry that were dangerous. All of the compounds contained a six-membered benzene ring, all had an amino grouping, and all also had an OH grouping. In normal urine and in urine of patients with vesical cancer some of the metabolic end-products resemble this common factor, and are principally a result of tryptophane metabolism. Price and collaborators have made studies of the tryptophane metabolism of the cat, since this animal is seemingly immune to bladder cancer. They found that trytophane is metabolized to amino hippuric acid in this animal; whereas in humans and in other experimental animals it is metabolized to kynurenine or anthranilic acid.

In 1954, Boyland and associates suggested a possible mechanism for the development of vesical tumor. In their opinion, if an aminophenol in the urine were conjugated with glucuronide but could still be split by a bladder enzyme into a free form, with sufficient time and concentration, such a mechanism could induce tumor. They demonstrated an excess of glucuronidase in patients having a bladder tumor and in patients in whom vesical tumors had been cured or arrested. As recently as 1956, Boyland and Watson implanted chemicals directly into the bladders of mice, and produced tumors, with the metabolic aminophenol compounds that were proved to exist in excess in the urine of patients with tumors of the bladder.

With continued experimentation of this sort it may be that it will some day be possible by biochemical procedures to correct or affect inherent metabolic errors. By this means, carcinogenic end-products might be neutralized so that one possible etiologic agent would be under control. The theory of a chemical metabolic offender would seem worthy of consideration, since there is a high incidence of bladder tumors in male patients who have obstruction of the bladder neck or coincidental urinary stasis.

Diagnosis

In unified efforts to control cancer it becomes the responsibility of the urologist to utilize all currently available diagnostic procedures for the fullest possible clinical assessment of patients with bladder tumors. Detailed examination is, of course, essential before the therapist can determine a plan of treatment or decide upon the type of procedure to be employed.

Full appraisal of the patient is comparable to surgical evaluation; that is, it is made according to the particular findings for whatever type of tumor that may exist. First, a thorough history is imperative, and it is particularly important to ascertain whether any previous genitourinary disorder existed or whether any surgical or radiation therapy has been applied. In the event of previous treatment of disease of the genitourinary tract, full details are necessary. These would include the source of the therapy, whether biopsy studies were made, full histologic explanation, and clinical course up to time of arrival.

We study our patients in the following manner. Urine cultures are then taken on all patients before examination by instrumentation is attempted, in order to eliminate the possibility of sepsis. Second, pyelographic studies are necessary for information on renal function, ureteral stasis, or any filling defects. Sometimes cystograms will afford an explanation of bladder defects that are incompletely understood. The next step is cystoscopy, with the patient anesthetized. From this procedure

one learns the type of tumor, whether papillary or solid, the size of the lesion, whether the base of the tumor is pedunculated or sessile, and the condition of the mucosa adjacent to the tumor. The fourth procedure is biopsy. Specimens for microscopic study are taken routinely by resectoscope or by Lowsley forceps. Every effort is made to assure inclusion of bladder musculature at the base of the biopsy material, so that a more explicit pattern of the disease process may be available. After biopsy, bimanual recto-abdominal palpation is performed when the bladder is empty. The patient is anesthetized in order to insure complete relaxation, and the examination is carefully and critically conducted. By this means the examiner can determine with a great deal of accuracy the degree and amount of penetration of the bladder wall by tumor. He will also find out whether the tumor is palpable and mobile within the bladder, or palpable with infiltration, or palpable but with extravesical spread, while the tumor is still mobile in the pelvis; or whether the tumor is palpable but fixed to the pelvis.

At this stage of the study for evaluation it is our practice to ask the radiotherapist to be present, so he can become fully acquainted with the clinical issue, as well as become more skilled in palpation. The urologic surgeon can, by touch, evaluate the degree of involvement and the amount of extravesical extension sufficiently to express a clinical-surgical decision concerning the treatment program. With the radiotherapist he can decide the type and amount of therapy to be given. If cystotomy or segmental cystectomy has been attempted, it will be necessary at this stage of assessment to appraise the amount of bladder contraction or degree of obstruction at the bladder neck. If such exists it is important to determine whether it will interfere with therapy or will produce symptoms as a result of reaction to irradiation. Also, at this time it must be decided whether urinary diversion must be accomplished first, particularly if there is extensive involvement of the bladder wall, so that ureteral obstruction and hydronephrosis will result. In such instances irradiation therapy is indicated.

Treatment

At this time the assessment of the patient's condition is complete, the type, grade, and stage of tumor determined, and the coincident physical findings correlated. The nature of the procedure and the amount of radicalism or of palliation to be essayed is now definite as in a surgical evaluation. All patients with superficial or low-grade bladder tumors in the group reported were treated by transurethral resection only. There has been no segmental surgery or any other type of open operation in any of the cases in this series.

In planning supervoltage therapy, application to the empty whole bladder rather than to any part of it has been the aim. Baker's[5] demonstration of circumferential lymphatic spread of cancer cells along the muscle wall has influenced treatment procedures, in that external irradiation is preferred in instances which might previously have received interstitial or intracavitary irradiation. In studies of the whole organ in infiltrating cancer of the bladder, he pointed to the presence of malignant cells in the lymphatics of the entire bladder wall, and thus, in his opinion, radical surgery is the procedure of choice. In some patients more than 50% of the bladder circumference is involved, well beyond the limits of palpable or visible disease, and therefore radical irradiation is indicated. The entire series of our cases was treated with the cobalt-60 irradiator or the betatron. For the first year the two machines were used alternately, with the purpose of a comparison of the differences, reactions, immediate results, and individual tolerance. Actually, the observed results seemed to be fairly equal. Recently, however, the betatron has been found the more satisfactory because of more thorough volume distribution. The greater penetration makes it possible to avert the delayed fibrosis of subcutaneous tissue in the suprapubic regions which did occur in some of the patients who were treated with Co^{60}. The Co^{60} is now utilized for cases in which the anterior wall is involved and extension into the prevesical space has occurred.

In radical therapy of bladder cancer a minimal tumor dose was delivered of 6,000 roentgens in 5 weeks, using a three-field arrangement. The fields, one anterior in the suprapubic region, and two posterior at the level of the sacro-iliac joints ranged in size from 6 to 8 cm. to 8 by 10 cm. It is pertinent to state that use of different sizes of portals and varying degrees of angulation of the posterior

fields has been helpful in coverage for both the primary tumor and the possible prevesical extensions. When the tumor is believed to be limited within the confines of the bladder, one anterior portal of 8 by 8 cm. and posterior portals of 8 by 6 cm. are adequate for good coverage. Furthermore, in the betatron series, a modification may be mentioned that improves distribution and, to some extent, spares rectal damage. This consists of loading the fields with a ratio of 2:1 in favor of the anterior portal. In patients who have had previous suprapubic bladder surgery the minimal dosage may be reduced to 5,500.

In palliative therapy, utilized in instances of extensive disease involving the pelvic wall or node metastasis, patients were treated with either two parallel opposing fields, or with four fields, with the dosage limited to a total of 3,500 or 4,500 r. in from 3 to 4 weeks.

Reactions to therapy vary considerably. Usually by the second week of treatment there is an increase in frequency of urination and some dysuria. The symptomatology is apparently related to the previous history and the severity proportionate to pre-existent obstructive phenomena at the bladder neck. Such rectal symptoms as burning and mild tenesmus, with or without diarrhea, usually develop near the end of the 5 week period of therapy. Systemic symptoms have been slight in our series of patients, and no irradiation sickness was induced except for malaise and reduction of appetite.

Results

The team approach is of especial importance in the follow-up appraisals of the bladder cancer patient after irradiation. Meticulous and careful cystoscopic examinations are required to assess both clinical and therapeutic efficacy. The immediate bladder reaction is ascertained, and the accuracy of localization checked in this manner. After irradiation the bladder may be expected to present diffuse erythema of the entire mucosa, with pseudomembrane formation and gross edema, accentuated at the periphery of the tumor. The cystoscopic routine is established and such examination is performed at intervals of 1, 3, 6, and 12 months. It has often proved necessary to do cystoscopy with the aid of saddle-block anesthesia, as the majority of the patients had high-grade lesions,

TABLE 1

ONE HUNDRED CONSECUTIVE CASES OF BLADDER CANCER TREATED WITH SUPERVOTAGE
(April 1954—September 1956)

Sex		*Average Age*	
Male	82 cases	Male	60.9
Female	18 cases	Female	70.8
Radical treatments (Y fields—5,500-6,000 r. in 5 wks.)			64
Palliative treatments (4 fields—2 parallel opposing fields)			31
Symptomatic treatments (2 parallel opposing fields)			5
Betatron			62
Cobalt			38

including undifferentiated and squamous cancer that could be staged in the B-2 and C types. For a trustworthy estimate of therapeutic accomplishment it is imperative that each patient be examined under ideal circumstances. Also, the radiotherapist is present again for the examinations.

One hundred and fifty patients with carcinoma of the bladder were treated with supervoltage radiation at The University of Texas, M. D. Anderson Hospital and Tumor Institute. In this presentation, the number is limited to the first 100 consecutive patients upon whom at least 6 months' follow-up can be reported, from the last date on the last patient in the series, which began in April 1954. In table I the sex and age of patients are given. The majority were male. Sixty-four patients received radical treatment; 31 palliative therapy, and 5 were treated symptomatically. In the 5, the total dosages amounted only to the minimal level of the usual therapeutic dosage.

Table 2 includes the histologic classifications of the lesions. Four primary bladder tumors were adenocarcinomas. One originated in ectopic prostatic tissue and one in the bladder mucosa (probably on the grounds of cystitis glandularis). One was a mixed transitional cell and adenocarcinoma, while the last was a mucus-producing lesion that

TABLE 2

PATHOLOGY

Transitional cell carcinoma	75
Squamous cell carcinoma	14
Undifferentiated carcinoma	5
Adenocarcinoma of bladder	4
Papillary carcinoma secondary from renal pelvis	4
	100
Concomitant carcinoma of prostate	5

TABLE 3

CLASSIFICATION BY GRADE AND STAGE (ALL CASES)

Grade	Stage		
	Superficial A-B_1	*Deep B_2-C*	*Metatastic D_1-D_2*
Low I-II	22	4	2
High* III-IV	15	31†	26†
Total	37	35	28

*Includes squamous carcinoma and undifferentiated carcinoma.
†Adenocarcinoma.

originated from ectopic enteric glands. Four cases of papillary carcinoma, secondary from the renal pelvis, had received previous nephrectomy.

Table 3 includes complete classification by grade and stage of the entire series. In plotting the grades against the stage, it became apparent that most of the low-grade lesions were in superficial stages, while the high-grade lesions demonstrated a greater degree of infiltration of the bladder wall and a higher incidence of metastases.

Both squamous and undifferentiated carcinomas have been included in the high-grade group, since the clinical behavior of both follows the pattern of high-grade transitional cell carcinoma. The four adenocarcinomas were included in the same category, so that more than two-thirds of this series are in the high-grade group.

Tables 4 and 5 represent our dual classification of radical and palliative cases. Nearly all of the superficial lesions and the majority of the deep infiltrating tumors of the muscle received radical therapy.

In advanced pelvic disease, when the lesion had penetrated the bladder wall and extended into the perivesical fat, or in instances of distant metastasis, proved at the time of evaluation, palliative procedures were employed. Within this particular group, there

TABLE 4

RADICAL CASES (64)

Grade	Stage		
	Superficial A-B_1	*Deep B_2-C*	*Metatastic D_1-D_2*
Low I-II	21	4	1
High* III-IV	15	21†	2
Total	36	25	3

*Includes squamous carcinoma and undifferentiated carcinoma.
†Adenocarcinoma.

TABLE 5

PALLIATIVE (36 CASES INCLUDING 5 SYMPTOMATIC)

Grade	Stage		
	Superficial A-B_1	*Deep B_2-C*	*Metatastic D_1-D_2*
Low I-II	1‡	0	1
High* III-IV	0	10	24†
Total	1	10	25

*Includes squamous carcinoma and undifferentiated carcinoma.
‡Had concomitant adenocarcinoma prostate.
†Adenocarcinoma.

were 10 patients who had high-grade lesions in advanced stages and in whom it was necessary to use palliative technics because of poor general condition, previous irradiation and surgery, concomitant adenocarcinoma of the prostate, or coexistent complications in the urinary tract.

Table 6 contains the follow-up findings after 2 years on 26 patients who received radical therapy. Of the group 16 are alive after 2 years, and in 15 no bladder disease is present. In each classification the number of survivors for the group is shown in parentheses so the results can also be evaluated according to the grade and stage of disease. In the group with low-grade lesions in superficial stages 3 patients died of intercurrent disease. In each instance the bladder was free of tumor at the time of death.

In table 7, the results of one year follow-up studies are shown. Of 24 patients, 18 are alive, 16 of which are without evidence of bladder tumor.

In table 8, results of radical therapy in 14 patients are reported after a follow-up period of from 6 to 11 months. One patient is in regression, and in the other 13 (11 living and

TABLE 6

RADICAL TREATMENT (PATIENTS WITH 2 YEAR FOLLOW-UP)

26 patients	Alive at 2 yrs. (bladder free—15)	16
	Dead (6 lived longer than 1 yr.)	10

Grade	Stage		
	Superficial	*Deep*	*Metastatic*
Low	7†(3)	2(2)	1(1)
High	4 (3)	12*(7)	0

In parentheses: Number of patients alive 2 yrs.
*Including 1 adenocarcinoma alive at 2 yrs.
†3 died from intercurrent disease—bladder free.

TABLE 7

RADICAL TREATMENT (PATIENTS WITH 1 YEAR FOLLOW-UP)

24 patients	Alive at 1 yr. (bladder free—16)	18
	Dead	6

Grade	*Stage*		
	Superficial	*Deep*	*Metastatic*
Low	9†(7)	2 (1)	0
High	5 (5)	6*(4)	2(1)

In parentheses: Number of patients alive at 1 yr.
*1 adenocarcinoma alive at 1 yr.
†1 dead at end of treatment for intercurrent disease.

2 dead) the bladder was found to be free of disease.

In table 9, 36 patients in the palliative group are reported, with a follow-up period of from 6 months to 2 years. Eight patients survived for more than one year, and one for more than 2 years.

Table 10 shows the complications of radical therapy that developed in 29 patients (21 out of 54 males, and 8 out of 10 females). In 11 patients the minor complications were persistent cystitis, persistent proctitis, and bladder telangiectasis. Eighteen patients, had major complications. Rectal and bladder hemorrhage occurred in 11, contracted bladder in 10, ulcer of the bladder in 3, and rectal ulcer in two. There were 2 deaths from severe uncontrollable bleeding from the bladder and rectum.

In table 11 the factors that contributed to development of complications are presented. Four patients had been previously irradiated, and, of these, 3 had major complications. In 6 out of 10 instances, patients in whom contracted bladder was a complication had histories of cystotomy or partial cystectomy. In 6 instances of recurrence, placed in the radical group, it is interesting to note that 5 were in superficial lesions, and only one in a patient with a deep, penetrating lesion. All recurrences were managed by transurethral surgery, and, in each case, there was a marked delay in healing. In one case a severe cystitis

TABLE 8

RADICAL TREATMENT (PATIENTS WITH 6-11 MOS. FOLLOW-UP)

14 patients	13 bladder free (11 alive, 2 dead)
	1 in regression

TABLE 9

PALLIATIVE GROUP 36 PATIENTS (5-SYMPTOMATIC TREATMENT)

Follow-up Groups	*Survival*		
	2 yrs.	*1 yr.*	*6 mos.*
2 yrs. (14 patients)	1	4	2
1 yr. (12 patients)		4	4
6 mos. (10 patients)			6

developed, and in another a bladder ulcer.

Of the 8 patients having squamous carcinoma and who received radical treatment, 2 are alive after more than 2 years. There are 4 who have survived for more than one year, and 2 are doing well, less than a year after therapy.

Recurrences

The recurrent bladder malignancy after irradiation is often of high grade and infiltrates the bladder wall deeply and is difficult to estimate in the preradiated evaluation. It is our intent to resect and remove as much of the intravesicular tumor mass, as possible, by endoscopic means, before therapy is started, and never to open the bladder for such procedures. It is expected that the bladder volume will contract after irradiation of the bladder for infiltrative lesions. In spite of negative I.V. pyelography prior to radiation, we expect embarrassment of ureteral drainage when there is trigonal involvement. The optimum time of postradiation evaluation is between the fourth and sixth months, the time for critical review as to the degree of completeness of therapy and whether there is evidence of recurrence. This examination is made under saddle anesthesia, with careful cystoscopic evaluation of the bladder mucosa at the previous site of the tumor, as to its appearance and whether there is any tumor

TABLE 10

COMPLICATIONS IN RADICAL TREATMENT

29 patients	Male—21 out of 54 Female—8 out of 10	
Patients with minor complications (persistent cystitis, persistent proctitis, bladder telangiectasis)		11
Patients with major complications		18
Rectal or bladder bleeding	11	
Contracted bladder	10	
Bladder ulcer	3	
Rectal ulcer	2	
Deaths related to above complications		2

TABLE 11

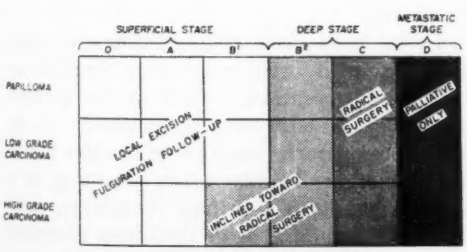
Previous irradiation—4 cases: 3 had major complications	
Contracted bladder—10 cases: 6 had previous cystotomy or partial cystectomy	
Recurrences—6 cases	5 superficial lesions 1 deep lesion
All managed by TUR	

present. An adequate biopsy is taken. Finally, recto-abdominal palpation of the empty bladder for evidence of extension or disappearance of bladder tumor in the bladder wall, or residual finding is done.

The management of bladder malignancies after irradiation presents two elements,—one of recurrence of the tumor with or without hemorrhage, and the other recurrence of hemorrhage bladder. In the case of hemorrhage from a postradiation ulcer, its location, or multiple areas of capillary oozing which may appear in many portions must be appraised. This usually is from the bladder dome, with the bladder mucosa itself offering entirely clear of tumor and no evidence of breakdown or denudation.

Management of the recurrent bladder tumor, providing the patient's condition is such to withstand operation, is complete cystectomy, nodal resection, and urinary diversion to the ileal loop, the Bricker technic. In instances of the serious bleeding from bladders after irradiation and without evidence of recurrence of tumor, we have been conservative to a fault at times in extensive replacement by transfusion, in an attempt to fulgurate bleeding areas endoscopically, and by irrigating the bladder with T e 3 solution at 12 to 14 day intervals, with only fair results. In the future it will be our policy to do a cystectomy and urinary diversion to an ileal loop in any case in which the blood volume has been replaced over a relative short interval of time without being able to control subsequent bleeding. Our cases have been of sufficient number and have extended over a long enough interval to have had a trial of palliative methods, and we feel justified in stating that surgical intervention for these phases of postradiated malignancies of the bladder are indicated. Those patients treated in this manner have done quite well in the immediate results now extending 6 to 16 months. Adequate time will be needed to see if the conditions will continue.

FIG. 1



THE INITIAL SURGICAL TREATMENT OF VESICAL NEOPLASMS.

In the cases we have observed and which have been referred to us after having had open bladder operations in an attempt to excise a tumor by fulguration with the radioknife and in spite of radical radiation when indicated, the results have been only palliative (Fig. 1). Once the bladder has been opened, whether for fulguration or partial cystectomy, the results have been universally poor. Radiation must be used for the extensive early metastases; cystectomy, of course, is of no value.

Summary

1. The early Grade I papillary tumor, noninfiltrative type, is approached best and controlled by endoscopic surgery, until there is a tendency of cellular conversion into a more active stage. Confirmation of extension by pathologic means may sustain the opinion obtained by recto-abdominal palpation.

2. The confirmation of the diagnosis being established by accepted methods, the degree and amount of infiltration into the bladder musculature determines the prognostic picture, as shown in our series of bladder tumor.

3. In all irradiated bladder malignancies with recurrence, providing the patient's condition will allow surgical intervention and the bladder had never been opened prior to irradiation, cystectomy and urinary diversion to an ileal segment have a definite place, and have proven to be quite adequate to our satisfaction.

4. When malignancy of the bladder continues to bleed after irradiation and one is unable to control this, and if the patient can be prepared for operation, cystectomy should be done with urinary diversion to an ileal loop.

5. The results of supervoltage therapy of

bladder cancer over an approximately 4 year period has involved the teamwork of the urologist and the radiotherapist. The use of surgery after adequate radical irradiation gives promise of more complete destruction of disseminated cancer.

6. A proper and safe diagnosis of urinary bladder malignancy is by closed endoscopic approach, and never by opening the bladder prior to radiation therapy. A bladder once opened, with active mitotic cells ready to be loosened into the lymphatic and circulatory mechanism, defeats all efforts in an attempt to cure such cases.

7. Successful urinary diversion to ileal loops has a marked advantage in the management of these cases with lessened impairment of renal function and avoidance of infection. This is especially true in inoperable malignancy or those with extensive infiltrative lesions if opened prior to radiation.

Conclusions

1. In management of bladder cancer, it is imperative that agreement and understanding exist between the urologist and the radiotherapist from the beginning of treatment.

2. All patients were assessed clinically to meet the demands of urologic surgery as we understand them at present, and were treated by every available means, whether radical or palliative in intent. Limitation of surgical procedures to transurethral resection in those with superficial tumors of low grades of malignancy, and avoidance of surgical interference in patients whose disease was in Stage II and C classification, has allowed for the first time an actual estimation of the therapeutic value of supervoltage irradiation.

3. Sufficient evidence exists to warrant further basic research into the likelihood of a metabolic derangement as a causative factor.

4. Many patients whose clinical histories would place them in the category of inoperable cancer have been offered an extension of survival through palliative supervoltage irradiation.

5. In this series the clinical evaluation of bladder cancer patients before therapy has proved its value. By relieving obstruction of the bladder neck before irradiation, and by maintenance of bactericidal drugs throughout irradiation treatment, the incidence of complications has been kept to a minimum, and the amount of bleeding from telangiectasis has been greatly reduced.

6. From the clinical assessment procedures true contraindications to any type of supervoltage therapy were ascertained. When involvement of the whole bladder wall was discernible, with extensive invasion by the tumor, or bilateral intramural ureteral obstruction with concomitant hydronephrosis, urinary diversion could, in some instances, be profitably utilized. Diversion effected by ileal loop, and occasionally ureterostomy, before supervoltage therapy was attempted made it possible for some patients to receive uninterrupted radical therapy who would, otherwise, have been candidates for palliative procedures only.

7. Previous irradiation, of whatever type, proved in all instances to be dangerous insofar as subsequent supervoltage irradiation procedures were concerned, and major rectal complications were more likely to occur.

8. In the older age group women were found to react less favorably to supervoltage therapy than men.

9. Supervoltage therapy can serve effectively to eradicate and prevent recurrence in instances of tumor impossible of resection because of position, or when the grade of malignancy seemingly was increasing.

10. Finally, there is actually an encouraging therapeutic prospect as a result of the combined effort. Radical supervoltage irradiation has a definite place in the management of patients with cancer of the urinary tract, and this series has established it, even in the dreaded and unsatisfactory experiences of high-grade or undifferentiated lesions. The degree of penetration into the bladder wall is the prognostic denominator. The potential curability of tumors of the bladder remains a challenge, whatever therapeutic medium is employed.

In the high-grade, deeply infiltrative stage in type, with recurrence after irradiation, surgical intervention is used to the greatest advantage. Usually there is association of the usual postoperative reaction of bladder bleeding, sometimes bladder ulcer, persisting as a clinical handicap. To these cystectomy, careful nodal appraisal with ileal loop diversion will be offered in our future cases. Those to

whom we have offered this procedure have done well, with observation of from 8 to 14 months to date.

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Advantages and Application of Tubeless Gastric Analysis*

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The advantages of determining the secretion of free hydrochloric acid by a dye excreted in the urine surely are obvious. However, this method still awaits the development of means of quantitating the acid.

GASTRIC ANALYSIS for the determination of free and total hydrochloric acid is a diagnostic aid in numerous conditions, including peptic ulcer, carcinoma of the stomach, and pernicious anemia. In 1950, Segal and coworkers[1] first described a simple test for determining free hydrochloric acid in gastric secretion by an indirect method. Their method was based on the release of quininium cation from a synthetic quinine carbacrylic resin by the free hydrogen ions in gastric secretion. Following the introduction of the qualitative method of tubeless gastric analysis, numerous investigators have reported their experience with the original quinine carbacrylic resin[2-9] and the newer azure A carbacrylic resin.[10-18] Previous studies have demonstrated a good correlation between the presence of free hydrochloric acid in gastric juice and the presence of quinine[2-4] or azure A[12,15,16] in the urine.

Stimulated by the easy availability and acceptance by patients of the tubeless method of gastric analysis, the present study was initiated to determine if the indirect method of gastric analysis could be quantitated.

Methods

Patients who were known to secrete free hydrochloric acid were selected for study. Two groups of patients, of approximately equal number, were tested. Each patient was tested twice—once with a tube method and once with the tubeless method of gastric analysis. All medications were discontinued at least 12 hours prior to the test.

Group I. Thirty-eight patients in Group I had a gastric analysis as the test is performed routinely at our Clinic. This procedure consisted of giving the patient 8 arrowroot cookies and 200 ml. of water at 7 a.m. after an overnight fast. One hour later a nasogastric tube was passed, and the contents of the stomach were evacuated. The gastric contents were filtered through gauze, and the filtrate was titrated with one-tenth normal sodium hydroxide for free and total hydrochloric acid using Topfer's reagent and phenolphthalein as indicators. The concentration of free and total hydrochloric acid was determined from the volume of one-tenth normal sodium hydroxide used in the titrations and was expressed as milliequivalents per liter. The quantity of free and total hydrochloric acid was calculated from the volume of gastric juice aspirated at one hour and the concentration previously determined. The quantity was expressed as milliequivalents.

On the following day the patient was tested with the tubeless method of gastric analysis. After an overnight fast the patient was given 500 mg. of caffeine sodium benzoate with 100 ml. of water. One hour later the patient was asked to empty his bladder, and this urine was designated as the control sample. Two grams of azure A carbacrylic resin* with 200 ml. of water then were given. All urine was collected for the next 2 hours and designated as the test sample.

The volume of urine passed in the 2 hour

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*Marketed as "Diagnex Improved" and supplied through the courtesy of Mr. G. D. Flake of E. R. Squibb and Sons, New York, N. Y.

test period was measured. A 10 ml. aliquot was acidified to pH 2 with 6 normal hydrochloric acid and boiled for approximately 20 minutes. The sample then was allowed to cool and stand at room temperature for 24 hours for the maximum color to develop. A portion of the aliquot was diluted 1:10. Using the control urine sample as a blank, the amount of dye in the test urine was determined with a Beckman D. U. spectrophotometer at a wave length of 620 millimicrons and slit width of 0.05 mm. The concentration of the dye in the urine was expressed in terms of milligrams per 100 milliliters of urine. The quantity of dye excreted in the 2 hour test period was calculated from the volume and concentration values and expressed as milligrams.

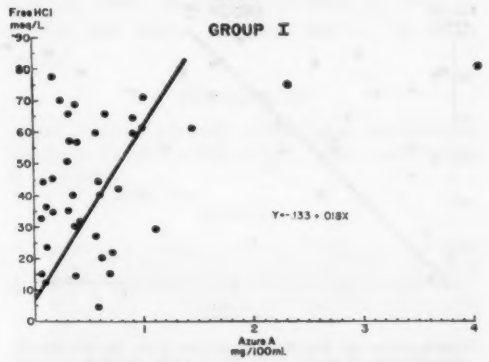
Group II. To produce high rates of gastric secretion for both the tube and tubeless method of gastric analysis, betazole** (3-beta-aminoethylpyrazole dihydro-chloride) was given to 30 patients who composed Group II. On the day that the tube method was used, betazole, 50 mg., was given subcutaneously to the patient. One hour later a nasogastric tube was passed and the gastric contents were evacuated. As with the modified Ewald meal used in Group I, total volume, and free and total hydrochloric acid were measured. On the following day the tubeless method of gastric analysis was performed. Again, betazole, 50 mg., was administered subcutaneously. One hour later the patient was asked to empty his bladder, and this urine was designated as the control sample. The patient then was given 2 Gm. of azure A carbacrylic resin with 200 ml. of water. For the next 2 hours all urine was collected and designated as test urine. The concentration and quantity of dye excreted were determined as previously described.

Results

The design of the experimental procedure allowed each patient to serve as his own control when the tube and tubeless methods of gastric analysis were compared. The quantity and concentration of both free and total hydrochloric acid obtained by the tube method were compared with the quantity and concentration of dye excreted in the urine when the tubeless method was used.

**Histalog, Eli Lilly and Company, Indianapolis, Ind.

FIG. 1

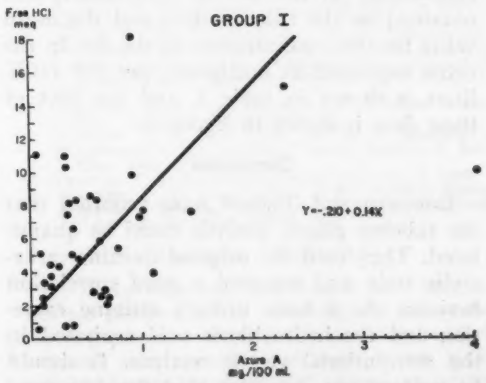


Scattergram obtained by plotting concentration of free HCl against concentration of azure A in the 2 hour urine sample. The equation expresses the slope of the line calculated from the data where X = mEq./L. of free HCl obtained with the tube method and Y = the mg. of azure A per 100 ml. of urine in the 2 hour sample.

Group I. When the quantity and concentration of both free and total hydrochloric acid, as determined by the tube method, were compared with the *quantity* of dye excreted in the urine, it was apparent that there was no correlation. However, when the concentration and quantity of acid obtained by the tube method were plotted against the *concentration* of dye in the 2 hour sample, the individual determinations tended to fall on a line as illustrated in figures 1 and 2. It is to be noted, however, that there was considerable spread in the scattergrams.

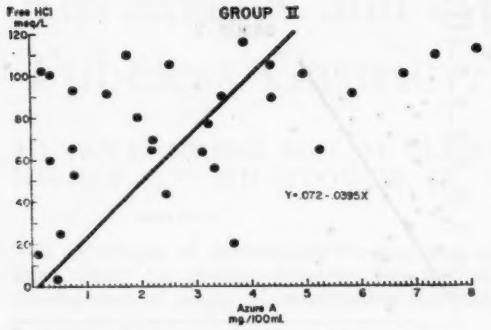
Group II. In this group similar results were obtained with the patients in whom betazole was used as a stimulus. Figure 3

FIG. 2



Scattergram of data when quantity of free HCl is plotted against concentration of azure A in the 2 hour urine sample. Equation indicates values of X and Y for slope of line.

FIG. 3



Concentration of free HCl in gastric juice plotted against concentration of azure A in urine when Histalog is given as a stimulus for both tests.

illustrates the correlation when the concentration of free hydrochloric acid was plotted against the concentration of dye in the urine. Again, it was noted that although the individual determinations tended to fall on a line suggesting a positive linear correlation there still was considerable spread of the individual points in the scattergram. When the patients were grouped in regard to the concentration of free hydrochloric acid secreted in response to betazole, a better correlation was obtained. The 30 patients composing Group II were divided into those who had a concentration of free hydrochloric acid below 50 milliequivalents per liter, those from 51 through 80 milliequivalents per liter, those from 81 through 100 milliequivalents per liter, and those whose concentration of free hydrochloric acid exceeded 100 milliequivalents per liter. The number of patients in each group and the mean value for milliequivalents per liter of free hydrochloric acid obtained by the tube method and the mean value for the concentration of the dye in the urine expressed in milligrams per 100 milliliters is shown in table 1, and the plot of these data is shown in figure 4.

Discussion

Donovan and Tighe[19] have reported that the tubeless gastric analysis could be quantitated. They used the original quinine carbacrylic resin and reported a good correlation between the 2 hour urinary quinine excretion and the hydrochloric acid aspirated in the conventional gastric analysis. It should be pointed out, however, that the data used in their correlation were pooled in that mean

TABLE 1

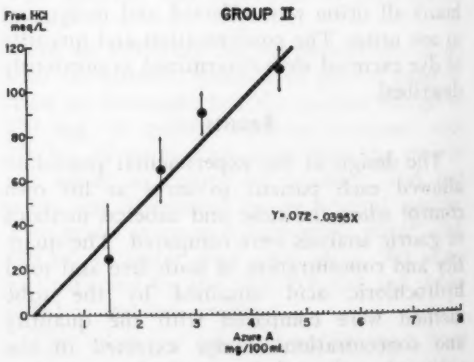
CORRELATION OF FREE HCl WITH MEAN URINARY AZURE A

Number of Patients	*Free HCl Range*	*(mEq./L.) Mean*	*Azure A (mg./100 ml.) Mean*
5	0- 50	23.4	1.450
10	51- 80	64.4	2.400
7	81-100	90.4	3.150
8	101-120	106.0	4.550

values for ranges of free hydrochloric acid were plotted against mean *concentration* values for urinary quinine.[20] Galambos and Kirsner,[21] using the new azure A carbacrylic resin with betazole (Histalog) as a stimulus, could find no correlation between the quantity of azure A in the urine and the quantity of hydrochloric acid in the gastric content.

These conflicting results may be explained by the fact that Donovan and Tighe related gastric hydrocholic acid to the *concentration* of the exchangeable cation in the urine; whereas, Galambos and Kirsner related the gastric hydrochloric acid to the *quantity* of exchangeable cation. Our data indicate that the concentration of the dye excreted is better correlated with the amount of gastric hydrochloric acid than is the quantity of dye excreted. Thus, our data can be used to support the results of either Donovan and Tighe or Galambos and Kirsner. Just why the concentration rather than the quantity of excreted dye is better related to gastric secretion of hydrochloric acid has not been explained. It may be that renal clearance is a limiting factor. We noted a marked variability in the

FIG. 4



A plot of the mean values of the concentration of free HCl over the ranges indicated by the vertical arrows against the mean values of the concentration of azure A in the urine.

volume of urine excreted during the test period. This probably explains why we were unable to obtain a positive correlation when this factor was introduced into the calculations. Many other factors probably account for the spread of the individual observations in our scattergrams. Pyloric obstruction or delayed gastric emptying, malabsorption in the small bowel, hepatic and renal disease, and obstruction in the lower urinary tract may interfere with the tubeless method of gastric analysis. These were avoided as far as possible in our patients. The fact that the tube and tubeless tests were performed on separate days could account for some of the variability we observed as low acid secretion and variations in gastric secretion may occur in the same person on different days. Other investigators[4,5,12] have reported that a quantitative relationship between the degree of acidity and the amount of dye excreted does not exist; however, most of these conclusions were based upon the determination of the quantity and not the concentration of the dye excreted.

At the present time the quantitative tubeless method of gastric analysis cannot be substituted for the tube method in the individual patient. However, as illustrated in figure 4, it may be that the technic of tubeless gastric analysis can be further modified and used to determine whether a particular patient is a hyposecretor, normal secretor, or hypersecretor. This would enhance the value of the test as a screening technic. Rosenthal and Buscaglia[18] recently have described a modification of their method of urine collection and have simplified their procedure by eliminating the test sample.

Summary

Tubeless gastric analysis is a reliable method for the detection of achlorhydria and for the qualitative determination of free hydrochloric acid. There is no correlation between the quantity or concentration of free hydrochloric acid secreted and the *quantity* of azure A recovered from the 2 hour urine sample.

There appears to be a correlation between the amount of hydrochloric acid in the gastric secretion and the *concentration* of dye in the urine.

Further modification and application of the quantitative tubeless method of gastric analysis seem warranted. It may be wise to collect the urine samples over a 24 hour period.

Acknowledgment

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Discussion (Abstract)

Dr. Robert McHardy, New Orleans, La. Dr. Laurens has presented a very interesting and provocative paper. Quantitative correlation of gastric hydrochloric acid and urinary excretion of azure A dye is intriguing. Kirsner has shown that there is no correlation between the quantity of urinary azure and the

quantity of hydrochloric acid in the gastric content.

The questionable value of tubeless gastric analysis is the detection of achlorhydrics in routine examination of asymptomatic patients in screening programs of the detection of carcinoma of the stomach and pernicious anemia. Published reports have documented the reliability of tubeless gastric analysis distinguishing those persons who do not secrete hydrochloric acid by the simple appraisal of a color change in the urine. Though persistent achlorhydria frequently is indicated by a negative test, it may result from a physiologic secretion variation or from inadequate secretory stimulus. It may be responsible for some of the poor results reported by some investigators.

In Dr. Laurens' results it is noted that there is a considerable spread of the individual points in the scattergram and better relation when patients were grouped. Therefore, the practicability of quantitative evaluation in the individual patient is questioned. Also, it is known that in the absence of maximal stimulation the basal gastric secretion may vary considerably from day to day in the same individual. Perhaps if the tests were performed on the same day, the periodic variation of the gastric secretory function may be reduced. Just why the concentration rather than the quantity of excreted dye is better related to the gastric secretion of hydrochloric acid is not clear. Factors other than the rate of gastric secretion appear to influence the excretion of azure A.

Dr. Laurens has stated although qualitatively accurate, the tubeless gastric analysis method is quantitatively inferior to intubation in the individual patient. However, if the presented method is substantiated, it may be applicable to those individuals in whom intubation gastric analysis is impractical or impossible because of psychogenic factors or esophageal abnormalities, and in whom the quantitative determination of acid is desired. In conclusion, it must be stated that the principal potential use of the tubeless gastric analysis with azure A is a screening procedure for achlorhydria when the qualitative result is all that is required.

Newer Agents in Dermatologic Therapy*

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The authors describe their experiences with a number of new therapeutic agents,—steroids, antibiotics, ataractics and the like.

IN RECENT YEARS many new preparations have become available for use in dermatologic therapy. The trend toward more cosmetically acceptable and clinically effective agents has been of increasing benefit to the patient and to a great extent has aided the dermatologist in his choice of medicinal agents. These new preparations have included products for local application and for internal administration.

An increased interest in new dermatologic products by pharmaceutical houses is apparent from their greater activity in this field. The careful and conservative clinical evaluation of new products should not prove a difficult problem, if in these studies full cognizance is taken of the multitude of factors capable of influencing the ultimate result and particularly its interpretation. There has been a tendency on the part of some to deprecate the publishing of the results of new product evaluation. This arises partly from the great number of these studies being published plus the fact that subsequent reports reveal that many agents do not warrant the original degree of enthusiasm. In spite of the crowded traffic along these lines, every effort should be encouraged that will bring new and better therapeutic agents to light. The proper medium is through carefully controlled, well-executed, and impartial studies that have been correctly evaluated. Criteria for the acceptability of investigative work of this type should not be so profoundly severe that it becomes impossible to estimate subjective reaction to therapy.

This report will present comparative studies of a number of new products, some of which have frequently been found effective in the management of pruritic dermatoses, pustular acne vulgaris, and the pyodermas.

Methods of Study

All studies were carried out on private dermatologic patients. Where possible double blind methods were used, or the drug being tested was controlled by treating the opposite symmetric area with a placebo of similar physical characteristics. The drug and placebo were used alternately if a single area was being treated. Cormia and Dougherty[1] have recently emphasized the many pitfalls commonly encountered in studies of this type. In the report contained herein every possible effort was made to circumvent errors attached to the human equation—prejudice, enthusiasm of the author, bias of the patient, as well as other factors that might lead to an incorrect interpretation of results. Where strikingly beneficial clinical effects were noted, an attempt was made to reconfirm the results by discontinuing the drug temporarily and re-employing it later. All statistical studies were prepared by nonmedical personnel who had only blind label control for drug or placebo identification.

Antipruritic Agents

Local agents. The local use of hydrocortisone and related corticosteroids has advanced them far into the lead as the most effective presently available topical antipruritic agents. Their clinical potential and effectiveness is increased by the fact that the index of sensitization to these drugs from repeated topical application continues to be very low.

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In this study of antipruritic agents the patients treated had either chronic forms of neurodermatitis-atopic dermatitis, nummular eczema, neurotic excoriations, infantile eczema, or seborrheic dermatitis. The predominant symptom was itching.

(1) Pantothenylol with and without hydrocortisone. The following preparations* were distributed at random among 451 patients with various pruritic dermatoses to be used topically three times daily: (1) comparative base cream, (2) Pantho-F 0.2% cream, (3) Pantho-F 1% cream. The applications of the three preparations were alternated at weekly intervals in a random fashion and continued as long as pruritus persisted. Pantothenylol (alcohol analog of pantothenic acid) has been reported to be an epithelial stimulant and to possess antibacterial and antipruritic properties following topical application.[2] The percentage of patients whose pruritus was decidedly benefited was 52%, 75%, and 71% respectively, for the comparative base cream, Pantho-F 0.2%, and Pantho-F 1% creams. In the same order, pruritus was neither benefited nor aggravated in 33%, 20%, and 24 per cent. The percentages of those whose pruritus became greater were 15%, 5%, and 5% respectively. In this study it is significant that the cream containing 0.2% hydrocortisone was approximately as effective as the 1% cream.

Patch tests were carried out later on those patients whose pruritus increased while being treated. None of these revealed evidence of sensitization.

(2) Prednisolone (Hydeltrasol) and Neo-Hydeltrasol lotions and ointments. In a study of 327 patients with a variety of pruritic dermatoses, the following preparations** were used topically: placebo lotion and placebo ointment, Hydeltrasol lotion and Hydeltrasol ointment, and Neo-Hydeltrasol lotion and Neo-Hydeltrasol ointment.

The lotion was used locally three times daily if the dermatosis was exudative, and was changed to the ointment preparation once the exudative phase had cleared. The placebo preparations were substituted at random intervals for each patient. The same preparations plus neomycin were utilized in the presence of primary or secondary infection. Both patient and physician were cognizant of the preparations containing neomycin. Once the infectious element was removed, the same preparations without neomycin were employed. Local therapy was continued three times daily as long as it was effective.

Of 327 patients treated, approximately 193 (68%) noted decidedly less pruritus, in 67 (24%) the degree of pruritus was not changed, and in 24 (8%) pruritus became more intense. Approximately one-third of those improved found the placebo preparations less effective. Among the patients who were not improved, there were a few complaints of mild burning and irritation, but no significant reactions of an allergic nature were noted.

(3) Metiderm Aerosols: A preliminary report. The local effects of two basic types of aerosol sprays* used as antipruritic agents were evaluated in a study of 127 patients with pruritic dermatoses. One type contained 50 mg. of prednisolone (Meticortelone) per 150 Gm. of aerosol spray. The contents of the second type were similar except for the addition of 57 mg. of neomycin sulfate.

An aerosol containing Meticortelone alone was used topically upon a variety of patients with pruritic dermatoses. A second aerosol containing Meticortelone and neomycin sulfate was used if primary or secondary pyogenic infection was present. No placebo substitute was employed in this group.

The medications were supplied in a metal spray dispenser with a capacity of 150 Gm. Patients were directed to spray the contents on the affected parts sparingly three times daily from a distance of approximately 3 to

*These preparations were supplied through the courtesy of U. S. Vitamin Corporation, Dr. Louis Freedman and Dr. Harvey S. Sadow. Comparative base cream—water-miscible (cetyl alcohol 15%, spermacetti 5%, glycerine 5%, oil in water emulsifying agent 1%, and water to make 100%) plus 2% pantothenylol (Panthoderm cream). Pantho-F 0.2%—comparative base cream plus 0.2% hydrocortisone. Pantho-F 1%—comparative base cream plus 1% hydrocortisone.

**These preparations were supplied through the courtesy of Merck, Sharp & Dohme Research Laboratories and Dr. John C. Richards.

Placebo lotion and placebo ointment contained the same bases as Hydeltrasol and Neo-Hydeltrasol lotions and ointments without prednisolone and neomycin.

Hydeltrasol lotion and Hydeltrasol ointment each contained 0.5% prednisolone 21-phosphate.

Neo-Hydeltrasol lotion and Neo-Hydeltrasol ointment each contained 0.5% prednisolone 21-phosphate plus 0.5% neomycin sulfate.

*The Metiderm Aerosols were supplied through the courtesy of Schering Corporation and Dr. G. Kenneth Hawkins.

The base of both types of aerosol contained per 150 Gm.: isopropyl myristate 5.25 Gm., and Freon 144.70 Gm.

6 inches, and to continue its use as long as it was beneficial.

Results following the local use of Meticortelone Aerosol on 56 patients showed: 42 (74%) with pruritus improved, 12 (21%) with pruritus unchanged, and 2 (4%) in whom pruritus became worse while under treatment. Similarly, following the use of Neomycin-Meticortelone Aerosol: of 71 patients 45 (63%) were improved, 19 (27%) were unchanged, and 7 (10%) thought their pruritus was increased.

Sensitization reactions were not encountered. No significant irritative reactions occurred unless the spray was used excessively. Prolonged application of the spray upon anyone, due to the refrigerant action, will result in vesiculation. Children were alarmed at times with the sudden application of the cold spray. Usually the chilling effect alone produced at least a temporary relief of pruritus.

The cosmetic acceptability to the patient as well as the ease of application were notable features. The use of the sprays upon intertriginous and hirsute areas seemed to be of particular benefit. The use of spray medication upon denuded areas diminished the trauma associated with local application. Although placebo control was not used, the results of these studies seemed sufficiently encouraging to warrant a preliminary report. Further development of this new approach in applying medicaments by a spray technic may significantly change and improve future dermatologic therapy.

(4) Oilated Aveeno. Most patients with pruritic dermatoses note an increase in pruritus after soap and water bathing. The beneficial effects of baths containing either starch or colloidal oatmeal are well-known. Solutions of hydrophilic colloids are considered to have a lubricating action through the retention on the cutaneous surface of some of the small particles of the colloid which may act as a lubricant.[3] However, the colloid particles of these preparations frequently leave the patient's skin quite dry after bathing, since they are usually hydrophilic and may increase the normal rate of cutaneous dehydration. To combat this drying effect, yet retain the colloidal action, colloidal oatmeal has been impregnated with approximately 35% liquid petrolatum and refined olive oil (Oilated Aveeno*). When this preparation is added to a tub bath the soothing effects of colloidal and lubricating action may be obtained.

Directions to patients: patients were instructed to avoid the use of soap. It was recommended that 3 to 4 rounded tablespoonsful of Oilated Aveeno be added to the water for a regular tub bath.

In this study 234 patients with generalized pruritic dermatoses were treated with Oilated Aveeno baths. These baths were added as adjuvant therapeutic measures and were continued once or twice daily as long as they proved beneficial to the patient.

Of the 234 patients treated, 186 (79.5%) obtained symptomatic improvement of pruritus, 34 (14.5%) did not think the medicated baths were of any greater benefit than nonmedicated baths, and 14 (6%) thought the baths might have increased their itching.

Systemic agents. Inasmuch as no local agent is completely effective in controlling pruritus in all patients it is frequently necessary to add auxiliary therapy by means of a centrally acting drug. Two preparations were tested,—meprobamate and procaine HCl.

(1) Meprobamate (Equanil** is a tranquilizer and its effectiveness is apparently related to a selective action on the thalamus and a blocking action on spinal interneurons.[4] Muscle-relaxant properties similar to those of mephenesin, to which it is related chemically, have been reported.

Meprobamate was administered orally to 131 patients in a dosage of 400 mg. three times daily. This was increased to as much as 2.4 Gm. daily if no beneficial effect was obtained. At the end of each 7 to 14 day period the medication was changed from the drug to the placebo, or if the patient began with the placebo, a change was made to the drug. Later, these changes were made at irregular intervals.

Of 131 patients, 91 (68.5%) thought their pruritic symptoms were decidedly less, 31 (24%) could not see that the oral medication helped, and 9 (6%) thought their pruritus was greater. Approximately 50% of the pa-

*This product was supplied through the courtesy of Aveeno Corporation and Mr. Sidney Musher, Vice President.

**Equanil was supplied through the courtesy of Wyeth Laboratories, Dr. Daniel L. Shaw, Jr., and Dr. James A. Page. Equanil is 2-methyl-2-n-propyl-1, 3-propanediol dicarbamate.

tients thought their itching was less while receiving placebo medication, however, an occasional patient concluded that the placebo was not as potent as the drug itself. The drug generally was noted to be more effective as a relaxing agent than as an antipruritic agent.

Most patients tolerated the preparation well and only six had to discontinue its use because of intolerance. Untoward side effects noted were initial sleepiness in three patients which continued as long as the drug was taken, nausea in two patients, and dizziness in one patient. Reactions in this group were not as numerous as those reported by Becker.[5]

(2) Procaine HCl (Ascorbacaine*). A total of 51 patients with pruritic dermatoses were included in this study. Each patient was given 4 capsules daily by mouth and this was increased to as many as 8 daily, if a favorable response was not obtained. At the end of the first 7 to 14 day period the drug was replaced by a placebo, or vice versa if the placebo had been used to initiate therapy. Subsequently, the two were alternated in an irregular fashion.

As a local anesthetic agent procaine apparently blocks transmission of nerve impulses by stabilization of the nerve membrane potential or by elevation of the threshold of excitability.[6] It has been shown that after oral administration of procaine, only minimal amounts are found in the blood stream.[7] Any beneficial effects may be partially due to diethylamino-ethanol, which has both analgesic and anti-allergic actions.[8] Both in the blood stream and tissues, procaine is quickly broken down into diethylamino-ethanol and para-aminobenzoic acid.

Ascorbic acid has been added since it may reduce the side effects of procaine.[6] It is doubtful that ascorbic acid alone exerts any primary antipruritic effect.

When Ascorbacaine was administered to 51 patients, 26 (50%) of the patients noted a decrease in itching, 21 (41%) remained unchanged, and 4 (8%) became worse. Adverse symptoms reported were nausea in two patients and headache in one patient. Under placebo therapy, approximately 40% of the patients thought their pruritus was diminished.

As an oral medication for the control of pruritus, this preparation is only slightly more effective than a placebo with the same physical appearance. The favorable results in this study were decidedly less than those reported by Luddecke[9] and Parish.[10]

An Antibiotic Ointment for Pyodermas

The present study concerns the local use of Neo-Polycin ointment.* It is prepared with a base called Fuzene which allows a rapid release of incorporated antibiotics and contains a small amount of polyethylene, a carbowax ester, and mineral oil.

This ointment contains: (1) neomycin sulfate, effective against most all gram-positive organisms except beta hemolytic streptococcus; (2) polymyxin B sulfate, active against *Pseudomonas aeruginosa;* and (3) bacitracin, active against beta hemolytic streptococci and other gram-positive organisms.[11] This combination provides an ointment with an unusually broad spectrum.

Fifty-five patients with primary or secondary pyodermas were treated, being directed to apply the medication locally over the involved areas twice daily as long as a favorable response was noted. If a favorable response was not obtained in 7 days, the preparation was discontinued, and the clinical effect considered unsatisfactory. There is some doubt as to the justification for the use of a local inactive placebo as a control in a human group with known pyogenic cutaneous infection.

Of 55 patients treated locally, 39 (70%) were improved within a 7 day period and the improvement continued, 11 (20%) remained unchanged, and 5 (10%) became worse while under treatment. The term improved indicated objective evidence of local decrease in erythema, crust formation, and purulent discharge. No sensitization reactions occurred in this group.

Tetracycline With and Without Steroids in the Treatment of Pustular Acne Vulgaris

The pustular phase of acne vulgaris frequently proves resistant to routine methods of treatment. The fact that systemic antibiotic

*Ascorbacaine Capsules were supplied through the courtesy of Testagar and Company, Inc., and Mr. M. S. Herman. They contain ascorbic acid, U.S.P., (150 mg.) and procaine hydrochloride, U.S.P., (250 mg.) and 150 mg. of lactose per capsule.

*Neo-Polycin ointment was supplied through the courtesy of the Pitman-Moore Co., and Dr. Philip A. Boyer, Jr. Neo-polycin contains in each gram, 3 mg. of neomycin sulfate, 400 units of bacitracin, and 8,000 units of polymyxin B sulfate in a Fuzene base.

therapy is beneficial in certain cases of pustular acne vulgaris has been established.[12-14]

Interest has recently been stimulated in evaluating the role of the adrenal steroids plus antibiotic agents in bacterial inflammatory processes. The present study was evolved to test this combination in the systemic treatment of pustular acne vulgaris.

A comparative double blind label evaluation effect of tetracycline alone, tetracycline plus prednisolone, and tetracycline plus 6 methyl prednisolone in the treatment of severe pustular acne vulgaris was determined over a prolonged period.

Bacterial culture and sensitivity studies were carried out in all patients unsatisfactorily responsive to both steroid and antibiotic administration. From approximately 10% of this group, *in vitro* bacterial studies revealed organisms resistant to tetracycline. It was also noted that approximately 10% of the patients with bacterial growth resistant to tetracycline improved, nevertheless, with antibiotic-steroid therapy.

During this study all patients had been maintained on routine therapy for acne for at least eight weeks.* If the pustular phase of their disease had not responded favorably, routine therapy was continued, but in addition each patient was given orally each day 1 to 4 capsules containing either tetracycline or tetracycline plus a corticosteroid compound. The four different capsules** being tested contained:

(1) 250 mg. tetracycline phosphate.
(2) 250 mg. tetracycline phosphate.
(3) 250 mg. tetracycline phosphate plus prednisolone, 5 mg.
(4) 250 mg. tetracycline phosphate plus 6-methyl prednisolone (Medrol) 4 mg.

The dosage and duration of this oral therapy was determined by the severity of the pustular phase as well as the responsiveness to treatment. The patients were re-evaluated every 7 to 14 days and their oral medication was alternated in a random manner every 30 days.

Since the proper identity of these drugs was unknown to the investigators as well as the patient, a supplemental supply of identified tetracycline was administered to those patients in whom a known contraindication to the usage of C_{21} steroids existed.

Tetracycline plus adrenal steroids and tetracycline alone were administered to 331 patients with severe pustular acne vulgaris over a 24 month period. Of the 331 patients, 263 (79%) of the entire group were improved, 56 (16.5%) remained unchanged, and 15 (4.4%) worsened while under therapy. Of 179 patients receiving tetracycline alone 139 (77.6%) were benefited. No appreciable difference was noted in the comparative clinical effects of tetracycline plus prednisolone and tetracycline plus methylprednisolone. The prednisolone-antibiotic combination benefited 60 (81%) of the 74 patients treated and the methylprednisolone-antibiotic combination benefited 64 (82%) of the 78 patients treated. The term improvement signified objective evidence of decreased inflammatory and pustular activity.

It is apparent that the combination of steroids plus tetracycline as utilized in this study was statistically of no greater value than tetracycline alone.

Comments

Certain general observations become clear after the evaluation of studies of this type. (1) The better dermatologic preparations should benefit at least 3 of 4 patients. (2) Since placebos may improve as many as 50% of those patients treated, any preparation that does not, therefore, prove beneficial to more than 50% of the patients treated probably does not merit further clinical usage.

At best, the clinical evaluation of dermatologic agents represents rough estimates rather than highly accurate calculations. With this in mind it should be possible to rate the effectiveness of some of these clinical agents if broad qualifications are used. Accordingly, the agents tested in these studies were assessed in this manner: As topical antipruritic agents the Pantho-F creams, Hydeltrasol ointment and lotion and the Metiderm Aerosols were sufficiently beneficial to warrant further clinical usage. Oilated Aveeno was usual-

*Dietary restrictions, office removal of comedones, ultraviolet light therapy, local application of Sulforcin lotion (Texas Pharmacal Co.) and meticulous cleansing of face and scalp with soap and water.

**These medications were furnished through the courtesy of The Upjohn Co. and Dr. Andrew J. Moriarity.

(1) Panmycin Phosphate (clearly labeled)
(2) Panmycin Phosphate (blind label)
(3) Panmycin Phosphate with prednisolone (blind label)
(4) Panmycin Phosphate with methyl prednisolone (Medrol) (blind label)

ly of benefit to those patients as an antipruritic agent where a bland lubricating bath was indicated. Equanil which qualifies well as a tranquilizer did not appear to be a superior systemic antipruritic agent. Ascorbacaine, as a systemic antipruritic agent, was only slightly more effective in this study than the placebo. Neo-Polycin ointment was usually found to be an effective preparation when used in the local treatment of pyodermas. The oral administration of a combination of tetracycline and prednisolone or tetracycline and methylprednisolone as utilized in this study was no more effective in treating pustular acne vulgaris than when tetracycline was used alone.

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Discussion (Abstract)

Dr. Arthur G. Schoch, Dallas, Tex. Opening the discussion of a paper presented usually follows one of several avenues. The discusser at times agrees wholeheartedly with the essayist, casting out verbal accolades and compliments, primarily because the two agree. Another type of discusser who is in complete disagreement with the essayist spends his allotted time violently disagreeing with that which has been said, point by point. A third type of discusser spends more than his allotted time ostensibly augmenting the essayist's thesis by presenting additional data (unfortunately usually augmented by slides) and frequently on such a tangential point that it is difficult to integrate the discusser's words into the main thesis. At this meeting I feel no obligation to adhere to any one of the three orthodox methods. "That's what I like about the South."

Dr. Noojin has packed into one paper a wealth of material, much of which is highly significant. It could easily be divided into five or six separate studies, carrying the Roman numerals between one and six, and be published separately and individually. My commendations, therefore, I believe are just because he has telescoped much information into one presentation.

Conspicuous to me, however, was the fact that of the products investigated for local application, many of which contained neomycin, there was no reported evidence of sensitivity acquired, or otherwise to this particular antibiotic. Considering the size of the series of cases here reported, it is almost unthinkable that not a single incident of neomycin sensitivity was observed.

In this paper there was no mention of trimeprazine (Temaril) as an antipruritic pill. In addition, there was no mention of triamcinolone or methylprednisolone, the 1958 model steroids, administered orally or locally. The previous speaker, Dr. Harry M. Robinson, Jr., has ably discussed the usefulness of triamcinolone. We have previously published preliminary observations on Temaril, Aristocort and Kenacort (triamcinolone) and Medrol (methylprednisolone). All three, administered by mouth, have certain outstanding value in the management of inflammatory dermatoses. Aristocort topical cream and Medrol ointment have been available for experimental use for a number of months. I believe it is safe to say that both are extremely effective, at least as good as hydrocortisone applied locally, and in the occasional patient more acceptable, and objectively superior.

Our present impression is that of the three, Temaril is a sharp advance in controlling pruritus of the inflammatory dermatoses. We agree that the newer steroids, triamcinolone and methylprednisolone, are more effective than their predecessors, the delta compounds of cortisone and hydrocortisone. And, finally, that the local application of triamcinolone topical and methylprednisolone in ointment form, still in the experimental stage (Aristocort topical and Medrol ointment), are in a minority group more effective than hydrocortisone ointment.

Gout in Orthopedic Practice*

FREDERICK W. ROOK, M.D., *Arlington, Va.*

Gout is probably the most misdiagnosed of the arthritides. If the physician will have a healthy suspicion for this disease he will be surprised by its frequency.

THE APPEARANCE OF TWO CASES of hydrarthrosis of the knee which gave a clinical picture of infection but which showed a high content of uric acid in the synovial fluid, and which responded adequately to colchicine was the stimulus for this study.

Gout, a disorder of uric acid metabolism, is accompanied by arthralgia which is often manifested by an unusual response to a minimal injury, usually is accompanied by an elevation of uric acid in the blood, and responds promptly to colchicine or other medication for gout.

This study includes a review of 13,589 new orthopedic patients over a 5 year period, in which 83 patients were diagnosed as suffering from gout for a percentage of 0.6 per cent. This is quite consistent with the previous report by Masterson and Rook[1] which included 9,399 patients from August, 1953, to January, 1957, to disclose a total of 66 patients having gout with a percentage of 0.7 per cent.

All suspected cases have had determinations of blood urea nitrogen, fasting blood uric acid, sedimentation rate, complete blood counts and peripheral blood smear along with a control fasting uric acid. One laboratory technician was assigned to carry out all of the laboratory procedures on all patients in a routine fashion.

The average of the control serum uric acid in the fasting blood (Table 5), was no higher than 2.9 mg. per 100 cc. for either sex. The highest control over this 5 year period was 3.8 mg., the same for both sexes. The average serum uric acid in the fasting state in patients diagnosed as having gout was found to be 6.8 mg. in males and 5.6 mg. per 100 cc. in females. The lowest was 3.5 mg. for males and 3.2 mg. for females, which appeared to be inconsistent with our original premise for the findings in gout. However, these low figures represented only 3 patients. One had typical gout by x-ray study and previous history. The course of 2 patients had been followed for many years, and have had a proven history of gout for this period of time. If these 3 are excluded, the lowest blood uric acid found in the male was 4.6 and for the female, 4.3 mg. As can be seen, these are much higher values than in the control determinations.

Again, as was reported in the previous series, the highest uric acid level in men was 10.2 mg. and in women, 7.8 mg. Women, in both series have tended to have lower levels of blood uric acid and do not have the florid manifestations generally shown by men, though in either case the response to colchicine has been most gratifying.

Of interest, is the fact that 17% of the patients gave a definite history of trauma which appeared to be a precipitating factor.

Table 1 shows the incidence of gout in orthopedic practice. Of a total number of 13,589, 83 patients (0.6%) were diagnosed as having gout. Of these, only 7 had been previously so diagnosed.

Table 2 shows the features of age and sex. The incidence in women in this series is much higher than in the present literature. Out of 83 patients, 22 were female for an incidence of 27%, whereas many reports have given an incidence of approximately 5 per cent. Also, of interest is the age range in which the great-

TABLE 1

GOUT IN ORTHOPAEDIC PRACTICE

Total No. Patients	%	*Total Number Diagnosed As Gout*	%	*Number Cases Previously Diagnosed*	%
13,589	100	83	0.60	7	0.05

*Read before the Section on Orthopedic and Traumatic Surgery, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

TABLE 2

CHARACTERISTICS—AGE AND SEX OF PATIENTS DIAGNOSED AS GOUT

Age Range Total—83 Patients	*Sex* *Male*	*Female*
20—29	2	2
30—39	15	3
40—49	18	8
50—59	17	7
60—69	7	1
70—79	1	1
80—89	1	
Totals	61 (73%)	22 (27%)

est number of patients of both sexes appear, between 30 and 60 years.

Table 3 shows the location and distribution of the symptoms and findings. This reveals there were subjective findings in some patients without objective findings. Of the total number of 83 patients, only 9 had definite positive x-ray findings consistent with gouty arthritis. The foot and knee regions were found to be most commonly affected, both subjectively and objectively in this series.

Table 4 contrasts the laboratory and clinical findings in the 83 patients. All but one patient gave the symptom of arthralgia. Only in 3 cases were there tophi. Eighty patients, or 96%, were found to have a definite elevated fasting blood uric acid, and those cases in which this did not occur, a previous diagnosis had been established. Sixty-four per cent of the patients had an elevation in the sedimentation rate.

Table 5 shows the specific findings in the

TABLE 3

LOCATION AND DISTRIBUTION OF SYMPTOMS AND FINDINGS

Joints Affected	*Subjective*	*Objective*	*Positive X-Ray*
Foot	33	21	3
Knee	15	14	
Big toe	9	9	2
Multiple	14	5	
Hand	7	7	3
Ankle	7	7	1
Elbow	1	1	
Hip	1		

TABLE 4

CONTRASTING LABORATORY AND CLINICAL FINDINGS IN THE DIAGNOSIS OF GOUT—83 PATIENTS

Total Number Arthralgia		*Total Tophi*		*Total Positive X-Rays*		*Total Elevated Uric Acid*		*Total Elevated Sed. Rate*	
No.	%	No.	%	No.	%	No.	%	No.	%
82	99	3	3.6	9	11	80	96	53	64

laboratory data in regard to range and average reading. In those diagnosed as having gout, the range of the fasting blood uric acid was from 3.5 to 10.2 mg. in men, and 3.2 to 7.8 mg. in women. If the 3 cases mentioned above are excluded from the total of 83, the range extends from 4.6 to 10.2 mg. in men and from 4.3 to 7.8 mg. in women. The sedimentation rate ranged from 2 to 55 mm., the lowest of 2 being in one man and the rate of 55 in 2 women. The average was 22.2 mm.

In *conclusion,* it is my opinion that the average normal fasting blood uric acid is considerably lower than given in most textbooks, and that any elevation above an empirical figure of 4.0 mg. per 100 cc. should be considered an indication for investigation since it denotes a definite tendency toward a disturbance in uric acid metabolism.

It would appear from this study of 13,589 patients that the incidence of gout is 0.6 per cent.

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1. Rook, F. W., and Masterson, J. H.: The Incidence of Gout in Orthopaedic Practice, T. Virginia M. Month. 85:28, 1958.

Discussion (Abstract)

Dr. Darius Flinchum, Atlanta, Ga. I wish to thank Dr. Rook for reminding us of the existence of gout in orthopedic practice. One would think the incidence would be a little higher than 0.6 per cent. It is also interesting to note that only 7 of his 83 cases of gout had been previously diagnosed. I have noticed, too, that people with gout have often had their symptoms for several years. It can also occasionally be present in quite young people and even in the teen-age group. Certainly we do see patients with uric acid levels in the upper limits of normal and yet symptoms of gout are present. In these people, if they show a dramatic response to colchicine, a presumptive diagnosis of gout must be made.

TABLE 5

LABORATORY DATA SHOWING SPECIFIC FINDINGS RE: RANGE AND AVERAGE READING

Uric Acid in Gout (100%)				*Uric Acid Controls (100%)*				*Sed. Rate-Gout (100%)*		*CBC*	*BUN*
Range		*Average*		*Range*		*Average*		*Range*	*Average*		
Male	*Female*	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*				
3.5	3.2	6.8	5.6	2.4	2.5	2.9	2.9	2 (1 male)		N	N
to	to			to	to			to	22.2		
10.2	7.8			3.8	3.8			55 (2 female)			

Hydrochlorothiazide in the Therapy of Edema

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The effectiveness of the sulfonamide diuretics has been established. This will lead to continued search for variants of this chemical group which not only may be effective but also be associated with a minimum of side effects. This paper describes the results in the use of one of this group of compounds.

HYDROCHLOROTHIAZIDE* is a new orally administered nonmercurial compound possessing strong diuretic properties. Chemically, it is derived from a benzene disulfonamide, being the dihydro derivative of 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine - 1, 1 - dioxide and has been given the generic name, hydrochlorothiazide. It, therefore, belongs to the group of sulfonamide compounds showing diuretic activity.

Pharmacologic studies upon hydrochlorothiazide indicate that it is a very potent diuretic substance, effective and well tolerated by mouth and possessing a low degree of toxicity.[1] In a recent review of the chemistry of the diuretic drugs, Sprague[2] reported on a new series of sulfonamide compounds, the most active of which was 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1, 1-dioxide (chlorothiazide). Compared to chlorothiazide, hydrochlorothiazide is 6 to 8 times more potent and has a longer duration of action. It was also found to predominate over chlorothiazide in its ability to influence the excretion of water, sodium, potassium and chloride. Animal experiments indicate that it affects the diuresis of chloride to a significantly greater extent than does chlorothiazide.[3]

It is the purpose of this presentation to report the early observations of the diuretic effect of the compound, hydrochlorothiazide, in humans with demonstrable edema.**

Method and Material

Patients with manifest edema were selected from the outpatient medical clinic of the University Hospital and Hillman Clinic. The group was comprised largely of persons with congestive heart failure, but also included a few with cirrhosis of the liver, stasis or lymphedema, or the nephrotic syndrome. All had previously received instructions concerning the preparation and use of a low salt diet, and were following such a diet as closely as possible within their economic means. Most patients were taking diuretic drugs at the time of being taken into this study or had taken them in the past. All cardiac patients were digitalized. Thus, the one criterion for inclusion in this clinical investigation was the presence of demonstrable edema and the averred willingness to return at the frequent intervals necessary for close clinical observation. Unless considered detrimental to the individual's health, the previously prescribed diuretic therapy was discontinued and hydrochlorothiazide substituted in its place. In a few patients with anasarca, the injectable mercurial diuretic was continued in the same or a lesser dosage and hydrochlorothiazide added to the regimen. Patients not already upon diuretic therapy were started directly upon hydrochlorothiazide for their edema. The amount of medication prescribed was a 50 mg. tablet of hydrochlorothiazide twice or three times daily until edema was controlled, after which the drug was decreased to the smallest amount necessary to control edema, usually 25 mg. twice or three times daily. Patients were seen every 2 to 4 days early in the course of therapy, and this interval was grad-

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*Hydrochlorothiazide supplied as Esidrix-TM by CIBA Pharmaceutical Products Inc., Summit, N. J.

**This investigation supported by a grant-in-aid from CIBA Pharmaceutical Products Inc., Summit, N. J.

TABLE 1

Patient	Age	Race	Sex	Cause of Edema	Previous Diuretic Therapy	Diuretic Program with Hydrochlorothiazide	Number of Weeks on Hydrochlorothiazide	Total Weight Loss in Pounds	Blood Pressure Before Treatment	Blood Pressure After Treatment	BUN. Before Treatment	BUN. After Treatment	Electrolyte Abnormalities in mEq./L.	Toxic or Side Effects
1	46	C	M	CHF-adhes. pericarditis	Mercurial 2 cc. bi-weekly	50 mg. t.i.d. M. 25 mg. t.i.d.	24	18.5	120/80	110/80	17	20	Cl-93	Transitory decrease in appetite
2	47	C	M	CHF	Mercurial 2 cc. tri-weekly	50 mg. t.i.d. mercurial 2 cc. tri-weekly	3	0	110/80	108/80	39	Not done	Cl-90	None
3	60	C	F	CHF	Mercurial 2 cc. bi-weekly	50 mg. t.i.d. M. 25 mg. b.i.d.	21	7.0	170/90	180/100	12	14	None	PVC. and U. wave in EKG. suggest low K.K. normal at this time
4	47	C	F	CHF cor pulmonale	Mercurial 1 cc. weekly, chlorothiazide 250 mg. b.i.d.	25 mg. t.i.d. mercurial 1 cc. weekly	18	10.0	118/80	120/74	16	30	Cl-75 CO_2-34.7	Symptoms of hypochloremia
5	53	C	F	CHF	"Frequent shots" elsewhere	50 mg. t.i.d. M. 25 mg. b.i.d.	20	28.0	170/60	120/60	11	15	None	None
6	66	W	M	CHF-nephrotic syndrome lymphedema	Chlorothiazide 250 mg. b.i.d.	50 mg. t.i.d. M. 25 mg. t.i.d.	20	5.5	190/85	150/70	24	23	Cl-96	None
7	56	C	M	CHF	Mercurial 2 cc. bi-weekly	50 mg. t.i.d. M. 50 mg. b.i.d.	20	48.0	170/130	158/100	10	26	Cl-93	None
8	64	C	M	CHF	Mercurial 2 cc. weekly	50 mg. t.i.d. M. 25 mg. b.i.d. or t.i.d.	20	27.0	114/80	120/84	11	11	Cl-86 CO_2-36	Symptoms of hypochloremia
10	62	C	M	CHF-adhes. pericarditis	Mercurial 2 cc. bi-weekly, chlorothiazide 250 mg. q.i.d., acetazolamide 250 mg. 4 das./wk.	50 mg. t.i.d. mercurial 2 cc. tri-weekly	19	6.0	130/90	124/80	27	25	Cl-95	None
12	61	C	M	CHF	None in 4-5 weeks	50 mg. t.i.d. M. 25 mg. t.i.d.	17	11.0	134/80	140/64	10	16	Cl-96	None
13	65	C	F	CHF	Mercurial 2 cc. bi-weekly	50 mg. t.i.d. M. 25 mg. b.i.d.	16	9.0	168/114	132/96	31	20	None	None
15	65	C	M	CHF	Neohydrin 6 daily	50 mg. b.i.d.	15	5.0	130/40	140/55	17	23	None	None
16	45	C	M	CHF-stasis edema	Mercurial 2 cc. sporadically	50 mg. t.i.d. mercurial 2 cc. bi-weekly	15	6.0	148/80	140/80	10	14	Cl-89	None

17	47	C	M	CHF	Mercurial 2 cc. bi-or tri-weekly, chlorothiazide 250 mg. b.i.d.	50 mg. b.i.d. M. 25 mg. t.i.d.	12	9.0	140/100	155/100	15	15	Cl-92	None
19	67	C	F	CHF	Mercurial 2 cc. weekly	50 mg. b.i.d. M. 25 mg. b.i.d.	8	2.0	140/70	124/70	19	12.5	Cl-93	None
20	86	C	F	CHF	Mercurial 1 cc. q. 2-3 weeks	25 mg. t.i.d. M. 25 mg. b.i.d.	8	4.0	120/70	120/60	43	22	Cl-93	None
22	55	W	M	CHF	Mercurial 2 cc. tri-weekly	50 mg. t.i.d. mercurial 2 cc. tri-weekly	8	9.0	148/90	124/70	19	23	Cl-95	None
23	68	C	F	CHF	Mercurial 2 cc. weekly	50 mg. b.i.d.	8	7.0	190/116	180/90	23	25	None	None
24	71	C	M	CHF	Mercurial 2 cc. tri-weekly	50 mg. b.i.d. mercurial 2 cc. tri-weekly	4	26.0	220/130	90/60	87	139	Cl-92	None
25	65	C	F	CHF	Mercurial 2 cc. weekly	50 mg. b.i.d.	7	10.0	190/106	190/90	12	13	Cl-95	Enuresis
26	80	C	M	CHF	Mercurial 2 cc. weekly	25 mg. t.i.d. mercurial 2 cc. weekly M. 25 mg. b.i.d.	6	16.5	180/90	150/64	38	16	K-2.7	None
27	77	W	M	CHF	Mercurial 2 cc. weekly	50 mg. b.i.d. mercurial 2 cc. weekly	6	11.0	148/70	130/70	54	36	None	None
28	58	C	F	CHF cirrhosis	Chlorothiazide 500 mg. q.i.d.	50 mg. b.i.d. M. 25 mg. t.i.d.	6	16.5	128/80	114/70	14	10	None	None
29	59	C	M	CHF cor pulmonale	Mercurial 2 cc. bi-weekly	50 mg. t.i.d. mercurial 2 cc. bi-weekly	6	7.5	130/70	108/70	23	29	Cl-93	None
30	70	C	M	CHF	Mercurial 2 cc. weekly	50 mg. t.i.d. M. 25 mg. t.i.d.	6	20.0	170/90	100/70	48	40	Cl-92	None
31	70	C	M	CHF-stasis edema	Mercurial 2 cc. tri-weekly	50 mg. t.i.d.	6	2.5	170/100	160/104	38	24	None	None
32	70	C	F	CHF	None recently	50 mg. t.i.d. M. 25 mg. t.i.d.	5	11.0	132/88	150/90	74	38	None	None
33	65	C	F	CHF	Mercurial 2 cc. weekly	25 mg. t.i.d.	4	5.0	140/90	122/80	23	34	None	Enuresis
34	70	C	F	Lymphedema	Mercurial 2 cc. weekly	50 mg. t.i.d.	4	6.0	184/74	180/70	22	27	None	None
35	70	C	F	CHF	None in 2 months	50 mg. t.i.d. M. 25 mg. b.i.d.	4	6.0	210/86	180/84	18	24	Cl-93	None

CHF—Congestive heart failure
M—Maintenance dose

ually increased to weekly visits until maintenance of an edema-free or acceptable clinical state seemed accomplished, after which it was lengthened to 2 to 3 week intervals. Urinalyses, complete hemograms and cephalin flocculation determinations were done at the onset and at 8 to 12 week intervals. Blood urea nitrogen and electrolyte determinations were done at each clinic visit. A moderate elevation of BUN. initially was not taken as a contraindication to therapy with hydrochlorothiazide, but a rising BUN. during therapy was considered a reason for discontinuance of the medication.[4] Patients were weighed at each visit, and clinical observations made regarding the amount of edema. The blood pressure and pulse rate were likewise recorded at each visit. Any cardiac irregularity appearing during therapy was evaluated immediately by an electrocardiogram in conjunction with the electrolyte values at the time. Supplementary sodium, potassium or chloride were prescribed only for altered electrolyte patterns.

Results

At the present time of writing, 35 patients have been given hydrochlorothiazide for their edema. The course of 30 of these has been followed for periods of 4 to 25 weeks, and 13 of the 30 for 12 or more weeks. Of the remaining 5, 2 were promptly removed from the series because of uremia being evident upon the initial blood chemical study, and 2 failed to return after one clinic visit. The fifth patient developed a headache the second day of therapy. She attributed this to the tablets and refused further medication, although headaches had been present in the past.

Information concerning the remaining 30 patients is recorded in the accompanying table (Table 1). All patients but one (No. 2) showed some diuresis as evidenced by weight loss. This weight loss exceeded 3 pounds in 27, or 90% of the group. The total weight loss for the group was 350 pounds, or an average of 11.7 pounds per individual. Although Patient No. 2 professed to take his medication as prescribed, this was considered doubtful, and after 3 weeks it was deemed advisable to rely solely on parenteral mercurial diuretics which could be administered by visiting nurse.

Eight patients required injections of a mercurial diuretic along with hydrochlorothiazide. Two of these (Patients No. 26 and No. 27) might have compensated on hydrochlorothiazide alone, but because of their advanced age and elevated BUN. values, it was considered advisable to continue the mercurial and add hydrochlorothiazide in small dosage. The other six, Patients Nos. 4, 10, 16, 22, 24, and 29, have severe cardiac disease whose failure poses constant problems in management, and necessitates extensive diuretic therapy.

Analysis of the electrolyte determinations shows that there were three instances of definite hypochloremia with chloride levels of 75, 86, and 89 mEq./L. Two of these were in patients with cardiopulmonary disease,—Patient No. 4 with cor pulmonale due to extensive kyphoscoliosis, and Patient No. 8 with asthma and emphysema. Patient No. 4 had shown hypochloremia at times prior to therapy with hydrochlorothiazide. Patient No. 8 developed hypochloremia following a week of respiratory infection and uncontrolled asthma. In both, the low chloride value paralleled an increase in CO_2 level, 34.7 and 36, respectively. Each complained of severe weakness and increased dyspnea during this period, and improvement followed the administration of ammonium chloride and potassium chloride. Both continue to present problems in management, largely due to this tendency toward respiratory acidosis. The third instance of hypochloremia, Patient No. 16, occurred after 12 weeks of therapy with full dosage of hydrochlorothiazide (50 mg. t.i.d.) and bi-weekly injections of a mercurial diuretic in an effort to control extensive edema in the very crippled legs of an obese cardiac. He had no clinical evidence of electrolyte imbalance, although his chloride level was 89 mEq./L.

Fifteen patients showed chloride levels of 90 to 98 mEq./L. on one or more occasions during treatment. Three of these had chloride levels in this range prior to therapy with hydrochlorothiazide. These electrolyte alterations were unassociated with clinical symptoms, and the values returned to normal limits without corrective measures.

There were no values of sodium less than normal, and no clinical manifestations suggestive of sodium depletion. Only one potassium level was reported as abnormally low, 2.7 mEq./L. in Patient No. 26, a very feeble,

aged individual. He had no associated cardiac irregularity, and felt particularly well at this time. An electrocardiogram taken on Patient No. 3, because of an increase in number of previously present premature ventricular contractions, was suggestive of digitalis intoxication and low potassium, but the level of potassium taken at the time of the EKG. was 4.7 mEq./L. No other cardiac disturbances occurred during the investigative period.

The blood urea nitrogen levels were normal initially and remained so in 18 patients. It was elevated initially and returned to normal or near normal levels in 7 patients. Four individuals showed an increase in the BUN. during therapy. In 3 of these the elevation is slight, and treatment with hydrochlorothiazide is being continued with caution. The fourth patient, No. 24 with anasarca, pyelonephritis, and increasing uremia, repeatedly refused hospitalization. In spite of a BUN. of 87 mg. per 100 cc., hydrochlorothiazide 50 mg. b.i.d., was added to the diuretic regimen of Mercuhydrin, 2 cc. tri-weekly, in a desperate effort to lessen his edema which was causing painful blistering, ulceration, and serous oozing from the legs. A 26 pound weight loss occurred over a 4 week interval, with diminution of pain and less general discomfort. The BUN., however, continued to rise, reaching a level of 139 mg. per 100 cc. and hydrochlorothiazide was discontinued. The patient's condition continued to deteriorate; the BUN. was 153 mg. upon the last determination, and he died 2 weeks later.

There have been no significant changes in the hemograms or urinalyses in any of the group. Twelve patients have been followed long enough for a re-check of their cephalin flocculation determinations. Nine of these were normal and have remained so. Three were abnormal initially and showed normal or improved values during therapy, as might be expected with improved liver function secondary to control of chronic passive congestion.

Side effects were outstanding in their scarcity. One patient complained of a transitory decrease in appetite, which disappeared after 3 to 4 days. A number of patients showed a gain of true weight following the disappearance of edema and mentioned an improved appetite. Two patients complained of enuresis at the height of diuresis. There were no instances of drug idiosyncrasy or other manifestations of intolerance.

Discussion and Conclusion

From these data, it is obvious that hydrochlorothiazide is a potent diuretic agent effective orally, and capable of mobilizing fluid in edematous patients. All types of fluid retention studied responded to this drug, supporting the hypothesis that the pathologic retention of sodium and water by the kidney in heart disease, cirrhosis, and nephrosis is caused by similar mechanisms.[5] Mild to moderate renal insufficiency did not apparently interfere with the efficacy of hydrochlorothiazide, and marked diuresis also occurred in the single patient with advanced renal insufficiency to whom it was administered.

The number of patients exhibiting slightly diminished levels of plasma chloride, and the 3 instances of definite hypochloremia in this group, as compared to the normal levels of potassium encountered, corroborates the chloruretic effect observed in animal experiments[3] and suggests a difference in action between hydrochlorothiazide and chlorothiazide.

Patients show excellent tolerance to hydrochlorothiazide, and thus far no patients have shown refractoriness. These data also indicate that it compares favorably in potency to injected mercurial diuretics and reacts additively when the two are administered concurrently.

In an effort to make a valid investigation of the clinical properties of hydrochlorothiazide, the drug was prescribed on an uninterrupted schedule, and the patients were maintained on a low salt intake. Having established the chloruretic properties of hydrochlorothiazide in humans, it might be clinically more practicable to employ an interrupted schedule of administration and/or increase the salt intake. Added caution is indicated in prescribing this preparation to patients with chronic lung disease who, because of their disturbed pulmonary physiology, tend to develop low chloride levels spontaneously. In this type of patient, supplementary chloride as the ammonium and/or potassium salts should be given routinely if frequent electrolyte determinations are not possible.

Although the nontoxic injectable mercurial

compounds have greatly altered the clinical outlook and course of edematous patients, comparable oral preparations would be of immense practical value. This new compound, hydrochlorothiazide, offers promise as the most potent oral diuretic currently available, and one which compares favorably with the injectable mercurial diuretics.

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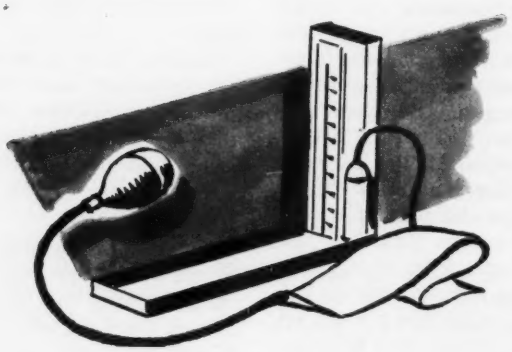

Hospital Treatment and Re-education of the Disturbed Adolescent*

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Little has been done in the past in providing for disturbed children and adolescents in psychiatric wards or institutions. There is a definite trend toward this type of management.

ADOLESCENCE cannot be avoided if growing up is to be achieved. Those whose living and work bring them into contact with adolescents undoubtedly have difficulty evaluating what represents disturbance and what represents normality in behavior. My own conception of the normal adolescent is a unique individual who is passing through a period of accelerated physical and psychologic growth. The everyday problems of the average adolescent are well-known to each of you.

Their behavior often includes extremes of all sorts. There are rapid fluctuations of mood, almost bizarre attitudes and frequent testing of the reactions of those around them. When these attitudes and fluctuations are taken seriously, the adult is often met with surprise and a meaningful look suggesting lack of understanding and stupidity.

My concept of the disturbed adolescent is more a quantitative than qualitative difference from the normal. These disturbances aroused by emancipatory drives, dependency needs, psychosexual immaturity, and pressures to conform may be in the form of more intense and frequent episodes. However, those who live with adolescents usually try patiently to wait it out hoping that "this too shall pass." It is when these young folk seemingly get caught in a constant repetition of disturbance, where emotional maturation seems arrested for long periods that one is asked to take a diagnostic look at the situation.

The decision as to whether an adolescent person should be admitted to a hospital is a very serious one in terms of what it means to him. In institutions for young people one observes that contacts with a psychiatrist are often looked on with the old-fashioned "crazy doctor" attitude. Furthermore, young people can be ruthless and cruel, giving undue harassment to their associates who receive psychiatric care. Therefore, hospital treatment has been reserved for that group whose behavior is so out of keeping with their environment, and so unacceptable to the individual, and so disturbing in the inner life that maturation is arrested in relation to the varying cultural standards.

The Norton Psychiatric Clinic hospital planners decided originally to pay specific attention to the needs of young folk and their treatment. Both the hospital setting and the program were adapted to this. During the first year after establishment of the Clinic 3 teen-agers were admitted. In comparison, 15 have come to the Clinic during the first 6 months of 1958, bringing the total adolescents treated in the hospital to 97 for the 8 year period since opening. These include patients of age 21 and below, all of whom showed predominance of teen-age or younger attitudes.

Norton Memorial Infirmary is a 300 bed private general hospital. The Psychiatric Service is a 33 bed unit, located on 3 floors. This includes a living area of 2 floors for the patient group and one floor for housing ancillary services such as doctors' offices, record room, gymnasium, music room, crafts shop and combination library and committee room. Not to be ignored is a beautiful roof garden for outdoor activities especially designed to avoid an offensive caged-in feeling.

In order to make the setting homelike there is no segregation of sexes by floors and there are attractive lounges, carpeted halls, wallpaper in the dining area, automatic washing

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machines and many other items to make living on the unit comfortable and homelike —a far cry from the violation of personal feelings so often associated with austere settings to which many have been and are subjected.

The staff consists of psychiatrists, both full-time and consultants, three advanced resident psychiatrists, psychiatric social worker, social group worker, clinical psychologist, a therapist with a Master's degree for arts and crafts and psychiatric nurses. Our psychiatric aides, with few exceptions are Seminary students in combination salaried service and training for academic credit. The total complement of personnel makes a personnel-patient ratio of approximately two to one. We think of all as members of a therapeutic team, and each team member is carefully oriented to accept the patient with his usual behavior, even though disturbed. All participate in evaluating interpersonal reactions so they may be used therapeutically. Daily meetings with personnel and weekly meetings with patient committees foster communication among all the groups.

The hospital population is made up primarily of ambulatory, treatable, voluntary patients of all age groups and both sexes. This tends to create a family grouping which is well suited for the interchange of attitudes and feelings, including those which are brought from previous life experiences.

The administrative functions of the psychiatric unit such as routine food service, maintenance and housekeeping are carried by the central hospital administrative staff with which the Medical Director carries on a close liaison, but this also gives him more time for attention to therapeutic program and teamwork. The personnel are constantly sensitized to the subservience of administration to treatment program. They take pride in the kind of organization which offers a high degree of individualized attention, even to that of providing a selective menu.

Every effort is made to preserve flexibility and an atmosphere of acceptance. Unnecessary rules and regulations are eliminated, and yet the patient is given the security of reasonable limits and orderly living. Philosophically the psychiatric treatment is eclectic, utilized in a truly modern setting with all the resources of medicine available within the same building.

Treatment begins with the first moment of contact. It continues as an everchanging interplay between the inner self of each patient, other patients, and personnel. Most persons with any awareness of illness are willing to participate or even make the decision to enter a treatment situation in the hospital if sufficient time and skill and sincere interest are available. In young folks this personal decision is often crucial as the beginning of treatment. Throughout the admission procedure and the hospital experience there is an attempt made to recognize and meet in a constructive way the feelings and attitudes of patient, referring physician and close relatives. During the first 24 hours there is constant companionship available through nurse or aide—one who knows the necessary answers to usual questions and can help a patient overcome the early anxieties, negative attitudes and fear. Adolescents particularly seem to appreciate this help through their initial awkward and often panicky adjustment period.

Following the change from home and initial reaction to admission with the get-acquainted period, there is usually a moratorium in the disturbed behavior. Shortly the newness wears off and, depending on inner pressures as well as environmental chance occurrences in the hospital group, the disturbed patterns of behavior emerge.

The therapeutic use of the hospital setting and hospital family is best demonstrated by presentation of two teen-agers with many similarities but a predominance of one type of behavior in each.

Case 1. Pat is a 14 year old daughter of very intelligent and creative parents. She is a physically precocious girl with poise and a high set of family values in spite of disorganized family routines.

Pat was accepted in the hospital because of increasing difficulty in concentration, recent thyroid disturbance, loss of interest, untidiness in personal appearance and vomiting in the morning before school. There was early rebellion toward the father, truancy from school and occasions when she would leave home and wander aimlessly at night.

Pat had been pushed prematurely into the role of housekeeper and caretaker of the large group of siblings while mother and father worked. She had not related well to the other teen-agers in her group but showed a strong competitive drive in intellectual ways.

Early observations on the reception service revealed a disregard for orderly living, physical restlessness and tension with inability to complete anything. This revolved around such simple items as cleanliness and care of clothing. There were marked shifts in mood. In addition there were confabulatory trends and a rich phantasy life.

During the previous year the attention to treatment of a suspected thyroid deficiency took precedence in dealing with Pat. In order to clarify the situation, complete physical studies including radioiodine uptake study were done. These revealed no abnormality and gradually were de-emphasized, since it was realized that they had been used as partial defenses. Considerable effort was necessary to work this through comfortably with the family physician and parents as well as with Pat in order to get a balanced treatment and perspective.

The denial of her female role was seen in Pat's lack of interest in boys, rejection of her previous homemaking ability, with neglect of feminine interests. Her ambivalence was seen in diet fads followed by excesses in eating. She set up her private castle in her room avoiding direct personal relationships. She was protected in this by a simple rule of no invasion of room privacy without invitation. Pat received empathy from the nurses who felt her family imposed on her, but the nurses soon found themselves in the same position of expecting her to do things and being made to feel she was being imposed on.

She refused orders but accepted explanations. She verbalized that she felt upset and angry at home but could not express these feelings except by wandering away and losing interest.

The father and mother participated freely in regular contacts with the social worker and occasional family discussions. Basic insecurities in the marriage came out and, actually, the mother exercised very little control. Pat repeatedly related how her father punished her in a physically embarrassing way. She seemed both attached to and fearful of him. She seemed to transfer this fear to the male psychiatric staff, but not nurses.

The family showed great concern over her statement that she wanted to "stay in the hospital for years." It was as if the hospital family met her needs and supplied her with a new type of independence free of major responsibilities. This early attitude toward sickness and hospitalization was a culturally acceptable way to punish her parents who were under financial pressure. This was also a convenient means of avoiding school.

Pat retreated into her private castle busying herself with books and magazines on love and romance. She listened to "rock and roll" music and avoided adult activities; however, she seemed to enjoy annoying them with *her* activities. This consisted of playing records and radio so loud that interactions with other patients and personnel were precipitated. At times like these there is a real test of the solidarity of the hospital family. There is delicate interplay of understanding, acceptance, limitation and the welfare of the total group. Such interplay varies from day to day with moods and attitudes brought from home to the hospital by members of the staff and all other personnel. This interplay has been well described in many of the writings of hospital milieu and group process. In Pat's situation even though the nurses were accepting her actions, the group was not and it became necessary to remove her records and radio on several occasions for short periods of time. It was observed that other teen-agers on the service at the time looked on with considerable satisfaction at this exchange between Pat and the adult group. Through the adult handling of this aggressive and somewhat negative behavior Pat became more secure with the personnel, even with limitations. She *joined* the teen-age group. This process of testing limits, finding out whom to trust and who was accepting Pat for her own sake, went on for a number of weeks with a very active communication which showed up not only in the ward situation but in the staff in its regular discussions outside the ward. Staff "father and mother figures" so-to-speak, were trying to maintain a growth-producing atmosphere for all of the group—not just for Pat.

Face-saving is important for everyone but for teen-agers it is a must. After a period of retiring to the room Pat found it easier to move out in the guise of an interest in craft shop to which she had been invited. It is often observed that there is less threat in the lack of directness of personal attention during concentration on an artistic project, than in either a general group experience or direct therapeutic relationship. Pat was helped back into the patient group through the craft shop relationships. Incidently, she developed considerable skill in painting. This helped remove the ideas which contributed to her original negative hospital activities.

In her preliminary hospital behavior one might readily observe similar teen-age activity in any home. During her hospital experience it was noted that another very important thing was going on: A rather shy, somewhat paranoid teen-ager who had been starving herself, risked her feelings in this interplay and became unthreatened enough to join forces with Pat in a very tangible reality testing. This is part of what we call patients helping each other, if the treatment setting and attitude of personnel will allow it. Improvement may happen more rapidly when the negative attitudes get on to the real issues of human relations instead of being shunted off onto bad food, unpleasant living conditions and artificial rules which are made only for the convenience of staff.

With limitations Pat often sulked and retired to her castle. The support of other teen-agers resulted in the establishment of teen-age group therapeutic sessions, in which they ventilated complaints with vivid feelings and communications. She was well established in the group as well as individual therapeutic sessions. Pat's female therapist found her anxious to get close and talk of more personal things. This could be described as a major breakthrough from arrested development to natural expression, resumption of learning, and willingness to see closeness to other human beings both on a negative and

positive level. This was followed by interest in getting back to her school books, a willingness to give up the idea of "years in the hospital" and a desire for home visits as well as contacts with her former schoolmates.

All during this period mother and father not only were aware of the facts of Pat's hospital experience but were somewhat gratified to see that meeting teen-age problems is not easy even for those who are supposed to "know." This was a great reliever of guilt for parents. They were able to discover that their own failure to meet each other's needs and inconsistency in behavior helped create an insecure family life which was a part of Pat's insecurity. Every stage of hospital progress was accompanied by a healthy change in the outside parental environment to which Pat would return.

Having reached security with her therapist, Pat was able not only to stand up to staff authority but to do this constructively. Her last flurry with authority and a test of the genuine attitudes of the nurses came with a vanilla extract "binge," collaborated in by her previously shy and withdrawn friend. There was so little negative resistance to it that she later reacted by saying, "Well, I guess I don't need to do those things any more."

The by-products of her more comfortable inner life were reflected in her increasing self-esteem. She took pride in her personal appearance, appeared radiant and an attractive teen-age girl, expressing new creative ideas. Residential hospital care was for a duration of 2½ mos., followed by a short experience of day care and gradual reintegration into her community environment. This was followed by occasional out-patient contacts.

Comment. In retrospect it appears that Pat had remained a little girl emotionally, doing everything she was told until normal teen-age strivings upset the balance. With her poor identification with females and a strong tie to her father, she did not know how to handle these feelings and felt different from other young people. In spite of her capacity for leadership she retreated and began developing feelings of failure. The hospital family created a new situation which allowed Pat to come out of her shell and be a normal teen-ager. We accepted enough of her behavior to help her not need her former unhealthy defenses and fostered her contacts with those her own age in group settings.

Along with these other evidences of maturation, interest in young men began to make the intense relationship with her female therapist seem less needed. Pat has made a crucial step in learning to live with herself and with others.

Case 2. Jim was a 17 year old white boy, the son of divorced parents. The father was a driving, aggressive and unpredicatble man who was quite well-to-do. Jim had been living with his mother, an attractive, seductive woman who had a young son by another marriage. The patient was an unwanted child, born when the mother was emotionally ill. His early care was mostly by his father and paternal grandmother. He was an intelligent child, sensitive and responsive to the difficulties in his parental environment. Early in life he learned to capitalize on the instability of his mother and the inconsistencies of his father, finding it easy to play one against the other.

His fear of his overpowering father, who during alcoholic episodes was inconsistent and financially generous, colored his relationships with others. He was emotionally wrapped up with his mother whose words suggested he should emancipate himself, but whose seductive ways and smothering attitude strongly tied him to her. With these relations with father and mother it was not surprising that he accepted warm masculine contacts not only from his doctor and minister, but also some devious older men to whom he became quite attached. Following his own recognition of the unacceptability of his set of values in his world he made several suicidal attempts.

Hospital admission followed his second suicidal attempt. He was accompanied by his father who offered to spare no expense but also demonstrated his tendency to control situations. Jim brought to the hospital memories of very exciting, tempting and yet guilt-producing experiences. There was also an attitude of hopelessness and verbal expression of determined suicidal intention.

Throughout his early hospital days he showed constant defensive projection blaming his mother and father for his plight and mistreated the "mothers" of the hospital staff, but with all of this seemed to be clinging to human contacts through an overpoliteness, rigid controls and verbalized proper values. He expressed some interest in the hospital chaplain. Jim was an aloof gentleman with the young ladies and young nursing staff and avoided the risk of closeness to the male personnel. As his security in relating to the hospital family increased he revealed more of his real feelings. These involved resentment and rejection of two teen-age female patients on the same hospital floor who were on a man-hunt. He became attracted to one of the male aides and communication was established with the aide before others of the senior staff. His insecurity with females of his own age was reflected further in his strong attraction to an elderly, very quiet and sensitive person old enough to be his grandmother, and with whom he continued correspondence even after leaving the hospital, calling her grandmother. It was as if he had discovered again safety and security like that of his infancy when cared for by his own grandmother.

After some weeks he became comfortable enough to justify increasing freedoms and a calculated risk in allowing him out of the hospital alone. He was somewhat careless with his money and like a small child overspent in buying a present for each person on the floor at Christmas. The response to this gesture resulted in a quietly conducted collection by the patient group who later presented him with a gift. This occasion seemed to be the turning point in Jim's

acceptance of the group and of himself. He began talking more freely with the staff psychiatrist and set him up as a go-between with his overpowering father. During this period he was able to express hatred for his father and lack of respect for his mother. There was much disgust, frustration and interplay of emotions regarding these relationships and during this time Jim became attracted to a young lady of his age who was visiting in from the outside. It is wonderful to see what love can do to an adolescent! Following a previous request to be moved from the floor where he might escape the pursuing females, he began requesting to go back to visit among them. However, following a small misunderstanding with his girl friend there was quite a reaction with expressions of suicidal intention, followed by an open admission of attraction to a male figure in the hospital. Jim had become comfortable enough to show his real feelings. The acceptance of his attitudes and an educational process allowing him to see that he was really struggling to get free of mother and grow up into manhood, was associated with a great deal of turmoil. During this period some of the very common impulsive wishes seen in teen-agers came out, such as wanting to get away from everything, buying an island and living as a hermit, stating people are no good. This was concurrent with an almost complete withdrawal to his room. People came to him with the same concern and interest which had been expressed throughout his stay. He questioned as to whether this interest was real and very shortly initiated spontaneous contacts with both patients and personnel. He took some time in deciding whether he was ever going to trust a woman again, but did show more maturity in his relations with women during one of his mother's visits. He seemed to accept the fact that women are in this world to stay. It was at this time his mother reacted most strenuously expressing concern as to whether he was going to return home with her and go to school, or return with the father, or worse—might he go away on his own? She wanted him to come to her, yet the divorced father insisted that she wanted this for her own financial security.

Jim's independence and self-confidence had been reflected for some time in his leadership among the teen-age group of the hospital. The young ladies eagerly followed his leadership in getting up a group petition to relax the limits on TV viewing. He was so sufficiently confident and adept with getting signatures to this petition that he obtained the names of several whose rooms adjoined the lounge and who had complained about late TV before!

While still living in the hospital Jim got himself a job in the community to establish some financial independence. He quit this in one week but with a fairly constructive attitude saying, "I got this on my own and I guess I have a right to quit it." He was supported in this although the father reacted negatively. About this same time Jim talked about more enduring plans, wanting to get back to his own former environment and to eventually re-enter school. There was considerable misunderstanding between father and mother in following separate communication on a long distance basis and finally it became necessary to send copies of letters to each. Following this they began to join forces so-to-speak emotionally in making plans with Jim. There was sufficient security developed between him and his parents and trust in the hospital family that he finally was able to leave the hospital and go on an interesting motor trip on his own initiative. He then returned to his environment with a fairly clear plan for himself.

After 6 months in the hospital his increasing assertiveness and expressions of reasonable opinions, dating and excitement about girls of his age reflected a real growth process. His behavior became more that of the happy teen-ager with spontaneity, a sense of humor and responsibility. He began dealing directly with father and instead of "taking him for all he could get," expressed ideas of moderation and financial accountability. In short, he seemed to be willing to become a man. Whatever else would seem to be in Jim's future in spite of a less-than-satisfactory parental adjustment, he has again become willing to enter life, meeting its problems and giving himself another chance.

Pat and Jim are only two examples of disturbed adolescents who in the external manifestations of their internal drives demonstrated many of the same attributes observed in delinquent, neurotic and psychotic individuals. It would be a grave error to try to catalog them according to diagnostic types rather than see them in an ever-changing dynamic growth process which has temporarily become arrested.

The hospital setting can contribute to the positive growth and self-esteem of those entering. The attitude of the personnel determines whether there will be both an individual and a group therapeutic environment. In the healthy hospital environment the hospital family is in a position to recognize personal problems and tempt the youth to come to grips with them in a meaningful way—a second chance to mature.

In order to make regression to childlike behavior and pseudomaturity unnecessary, treatment goals are best developed according to individual and environmental needs. Some of the guiding principles applying to everyone should be inherent in the hospital family setting.

1. Love of and respect for other human beings.

2. Acceptance of the idea of interdependence as well as independence.

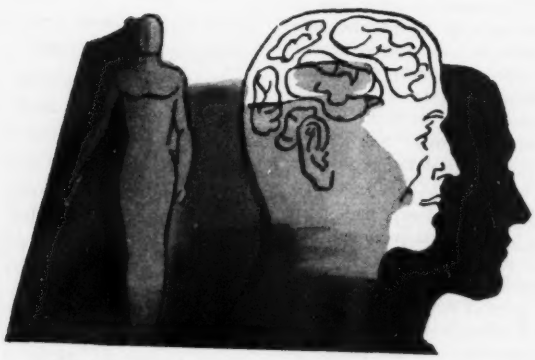
3. Freedom to disagree and respect for mutual agreement.

4. Flexibility in rules which must be adapted to individual differences as well as the group. Rules must be spelled out.

5. Recognition of each person's concept of himself and need to test his own values. These include such things as relative honesty, sexual behavior, religion and general interests.

6. Understanding of why parents behave as they do.

From our experience with disturbed youth, having followed some over many years, there is reason for examination of our treatment programs. In spite of the concept that illness in youth is prognostically disastrous, there is reason for optimism in the application of present knowledge because many can and will get well.



Hearing Loss Due to Industrial Noise*

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Conservation of hearing may be an important facet of preventive medicine in certain industries.

AT THE BASIS of the whole question of noise-induced hearing loss is one cardinal fact: Except for temporary shifts which occur after short exposures, this type of impairment is totally irreversible. The primary damage caused by acoustic trauma is destruction of the hair cells of the organ of Corti, structures which are essential because the fibers of the nerves of hearing terminate in contact with them, and also structures which have poorer powers of regeneration than any other organ in the body. Noise-induced hearing loss can be prevented, and its progression can be halted, but once nerve damage of any degree has occurred, the process is permanent and irreversible.

The education of management in this respect is part of the responsibility of the physician in industrial medicine. I regret to admit that my own endeavors along this line have not been successful.

In 1946, the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology became most concerned about the increasing problem of noise-induced hearing loss. The following year, a Subcommittee on Noise in Industry was set up for the specific purpose of studying the whole question of the relation of industrial noise to hearing loss. This Subcommittee has done outstanding work, including the establishment of a research center in Los Angeles, where a most cooperative staff is glad to help anyone who needs information or assistance of any kind.

Other organizations and groups have also studied the effect of noise on hearing, and there is increasing interest in the whole matter, as there should be in this age of increasing mechanization, jet propulsion, intercontinental and space travel, and other advances in industry and transportation. It is unfortunate that there is still exceedingly little interest in the circles in which interest is most needed and in which it would do the most good.

Analysis of Noise Exposure

A hearing conservation program, from the standpoint of noise-induced auditory impairment, falls into three parts. It consists of, a noise-exposure analysis; provision of control of exposure to noise; and measurements of hearing. Of these three components, the measurement of hearing is probably the most important.

An analysis of noise exposure is clearly indicated in any plant in which:

1. There is difficulty in communication by speech in the area of noise.

2. There are complaints of head noises or ringing in the ears after the worker has been in the area of noise for several hours.

3. There is transient loss of hearing that has the effect of muffling speech after several hours of exposure.

The absence of pain is a false and misleading criterion. It definitely does not mean that the noise level is not such as to cause hearing loss. Pain invariably occurs when the noise level reaches the level of 130 decibels, but heavy losses can be, and are sustained at considerably lower levels.

An analysis of exposure to noise is the only satisfactory method of determining the need for a program of hearing conservation in any particular plant. It is not a task for untrained personnel. It must be done by persons with training and experience in making measurements with special equipment, including sound level meters and octave band analyzers.

Industrial noise falls into two general categories. The first variety is *impact noise,* which consists of bursts of sound and is generated by such equipment as drop hammers, punch

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presses, and paper shredders. The second variety, *steady noise,* tends to fluctuate at irregular intervals but is continuous. It is generated by such agents as compressed air, diesel engines, and lathes.

A noise analysis should include information on a number of points in addition to the over-all level of noise:

1. The composition of the noise, in which the energy is practically never distributed uniformly through all the component frequencies. In noise from piston engines and pit furnaces, for instance, the energy is chiefly in the lower frequencies. In noise from pneumatic hammers and high-speed saws, on the other hand, the energy is in the middle and higher frequencies.

2. The duration and distribution of exposure during a typical work day. The greater the intensity of the noise, the shorter is the exposure needed to produce a hearing loss. When there is repeated or chronic exposure, the degree of auditory impairment depends upon the intensity of the sound,—the greater the intensity, the greater the resultant hearing loss.

3. The length of such interruptions as occur.

4. The spatial and environmental circumstances.

5. Reverberation of the noise, or absence of reverberation.

6. The total exposure during a work life.

Prevention and Control

Exposure to noise is best controlled in the environment by reducing the amount of noise produced at the source. Machines, presses, and other machinery can be mounted on cushions of cork, rubber, or some other resilient, sound-absorbing material. Machines that are particularly noisy can be tolerated, so the noise they create will affect the smallest possible number of workers. Some machines can be located in sound-conditioned rooms and be observed through windows. Special sound-absorbent materials can be used in the ceilings and walls. All of these expedients may be used, without too large an additional expenditure in new construction. They are completely impractical, at least *in toto,* in existing construction because of the extreme expense their institution would cause. Some of these methods, however, can be instituted in most plants, and even in plants of undesirable construction it is often possible to revise the operational procedure to reduce the exposure to noise. This can be done by rotating personnel, changing job schedules, and making the fullest possible use of remote control stations and observation booths.

The problem comes down, then, to the protection of the individual by the use of ear protectors to reduce the noise level at the inner ear. Dry cotton offers no protection whatsoever. Ear muffs are most useful as supplements to ear plugs, which may be made of rubber, neoprene, plastic, or cotton impregnated with wax.

To be most effective, ear plugs must be fitted and they must, of course, be worn regularly. They have undesirable features and it is difficult to make their use mandatory, but there is no more reason for their not being worn routinely in area of noise than there is for the omission of goggles in occupations dangerous to the eyes.

Auditory Testing

For the protection of both the individual worker and the employer, nothing is as important in the program of hearing conservation as the measurement of hearing. A pre-employment audiogram should be as integral a part of the pre-employment medical examination as is roentgenologic examination of the chest. If the environment is noisy, the examination should be repeated at regular intervals, and a postemployment examination, when the connection is terminated by retirement or otherwise, should never be omitted.

The preplacement tests are made primarily to establish the employee's hearing threshold at the time he begins his employment. The follow-up tests will record any changes in hearing resulting from age, disease, accident, or exposure to noise. They are most important in the protection of the worker from further loss of hearing. The postemployment examination is equally essential, for industry has no assurance that claims for industrial loss of hearing will not be filed as long after termination of employment as state statutes of limitations will permit.

The preplacement audiogram should be by air conduction, to determine the threshold for the frequencies 500, 1,000, 2,000, 3,000,

4,000, and 6,000 cycles per second. Bone conduction tests with masking procedures are not necessary. While prefabricated audiometric booths are inexpensive and more satisfactory, any reasonably quiet room will answer the purpose.

Testing of the hearing by air conduction audiometry for industrial purposes can be readily taught to any person of average intelligence. If, however, there is an average of 15 decibels or more of hearing loss at 500, 1,000, or 2,000 cycles per second, the employee should be referred to an otologist for a complete otologic examination and placement evaluation before he is assigned to a position.

At present there is no valid predictive test to detect ears which are highly sensitive to noise. The periodic follow-up test is the only way to detect them. The first re-check audiogram should be made not more than 30 days after the employee has been working in an area of excessive noise. To eliminate the element of fatigue, which could cause temporary changes in hearing, the test should be made at least 16 hours after the subject has been away from the noise; this period is sufficient for him to recover from any temporary shift of threshold he may have sustained from exposure. The first re-check and audiogram is really a study in the correct placement of the worker.

The periodic follow-up audiograms are screening tests, intended to show that the hearing at any frequency is as good as, or worse than, or the same as, any particular frequency at the screening level. If screening tests are properly conducted they are satisfactory for the periodic follow-up tests, which should be done at 6 month intervals. It is now recognized that if the loss at 4M cycles is not more than 50 decibels it is as great as, or greater than the loss at any other frequency. Therefore, screening at this cycle (4M) is a recognized screening method.

Workers who show a level below the screening level should be referred at once to an otologist for a complete study. Since most hearing losses induced by noise involve the 4,000 cycles per second frequency first, and this is not a frequency critical for speech, the follow-up test will detect losses in time to make the proper changes in placement before the critical frequencies of speech are damaged. Without follow-up tests these changes can go unnoticed until irreparable damage is done.

One of the values of the preplacement examination is the information which can be obtained concerning the previous history and its possible relation to hearing impairment which is detected. Hearing loss induced by noise is usually bilateral and audiograms are frequently symmetrical. Similar losses, however, may also be due to many other causes,—including bilateral otitis media; syphilis, chronic toxemias from dental, tonsillar, prostatic and other sources; drugs, particularly quinine and streptomycin; senile vascular changes, particularly arteriosclerosis; advanced otosclerosis, in which nerve damage eventually occurs; battle trauma or trauma from previous employment; presbycusis, which produces a loss of 5% at age 50 and of 10% at age 60, even in persons with supposedly unimpaired auditory function.

Summary

Hearing loss induced by noise is a problem of great industrial importance in this age of increasing mechanization, jet propulsion, intercontinental and space travel, and other advances in industry and transportation. Except for temporary shifts caused by brief exposure, the pathologic process which affects the hair cells of the organ of Corti is generally irreversible. The cardinal point of management is therefore prevention. A program of conservation of hearing falls into three parts, namely,—an analysis of exposure to noise; provision for control of exposure to noise; and measurements of hearing. The most useful work in this field has been done by the Subcommittee on Noise in Industry of the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology.

NOTE: This presentation has been taken almost entirely from the "Guide for the Conservation of Hearing in Noise," revised in 1957, and prepared by the Subcommittee on Noise in Industry of the Committee on Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology. Physicians and others interested in starting a program of conservation of hearing in any particular industry may obtain full information by writing the Research Center of this Subcommittee at 111 North Bonnie Brae Street, Los Angeles 26, California. The personnel of this center will be happy to advise on any problems encountered in the setting up of such a program.

Trends in Industrial Psychology*

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As a psychologist working in industry, my primary emphasis is upon prevention. I am sure all of us here have this in common as our guiding principle. However, realistically and practically this principle is more an ideal toward which we aspire and work, than an actual accomplished fact.

One of the assumptions basic to a preventive approach is that we work with people as people, and not merely as cut fingers to patch or as problems to solve. When viewed in the light of preventive medicine, management of the patient takes on a new meaning. From my own point of view there is a world of difference between treating the emotionally distressed man who knocks on my door asking for help, and the apparently well-functioning man who may not be doing as effectively and as comfortably as he might be, but who is not under enough stress to ask for psychologic help, or who may not realize that emotional factors may be affecting his day-to-day performance.

Health, be it physical or emotional, when viewed from the vantage point of prevention implies a cooperative effort. It means active participation between the doctor and the patient. The doctor may provide guidance, orientation, and a facilitating milieu, but the initiative must rest with the patient. In another sense, the doctor provides the motivation to overcome the initial inertia, but once the machinery is set into motion the patient takes increasing responsibility for its operation. To carry the analogy one step further, the doctor may "oil" the machinery now and again, but the hope is that his active participation becomes limited to that of supervisor and advisor. The patient has the major part in "running the show" opposed to the conventional role of management in which the doctor takes over. Of course, "taking over" is very much the physician's responsibility in the curative sphere.

On the emotional side, the main task is the recognition of tension in the many different disguises in which it may be manifest. To be able to do this effectively one must have a fairly sound orientation in the stress points in our culture and must have a sound understanding of what makes people "tick."

I would like to discuss several of the basic psychologic principles fundamental to the understanding of personality.

First, is the concept of normality. As the Maine farmer said when he saw the giraffe, "there ain't no such animal." The concept of normality flourished in the days of trait psychology which was prevalent in the twenties and thirties. We have outgrown this concept as our knowledge in the field of psychology advances. To illustrate, take the aggressive, out-going, "hail fellow well-met" high pressure salesman and contrast him with the rather reticent people, retiring research chemist or with the logical, precise, rationalistic, pedantic lawyer—which one is normal? It becomes immediately evident that normality is not a proper yardstick by which to evaluate these three essentially different behaving individuals. Rather it seems that we must have other yardsticks which cut across the different "personality types," and which do not attempt to fit individuals into preconceived molds, even though the molds have considerable latitude. It seems more proper to accept people as they are behaviorally and to ask, "How effectively and how efficiently do they discharge their day-to-day responsibilities, how comfortable are they, how happy are they, what sort of prices do they pay for their achievements?" Yardsticks of this sort seem much more appropriate. This means we can accept any kind of individual's behavior with reference primarily to the characteristic ways of dealing with the world around him, and to evaluate him as he is for what he is. Applying this reasoning

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to the preventive approach to medicine we would say, we are not interested primarily in the peculiar and idiosyncratic behaviors of an individual, but we are much more interested in the price an individual pays for getting along in his circle of activity.

Since I mentioned the characteristic ways of behaving it may be well to discuss this point next. In any culture there are a finite number of ways in which an individual is permitted to respond. A culture sets the boundaries and establishes acceptable and nonacceptable limits for the individual's behavior. This is a fortunate thing, for if everyone behaved as a law unto himself, there would be no way to classify and to describe human behavior. In fact, to pursue this point, if we were to say, for example, that an individual behaves in obsessive-compulsive ways, then we can presume that he must have had certain kinds of life experiences for him to have formulated this particular means of dealing with the world about him. In our present state of knowledge it is not easy to predict how this kind of person would behave in various situations, except in rather crude ways. In industry we are called upon constantly to make educated guesses regarding the kind of risk a man might be from both the physical and emotional aspects. As we gain more experience in this field undoubtedly our predictive batting average will sharpen.

Related to this notion of there being a limited number of ways in which a person can respond is the matter of diagnosis. In the area of diagnosis it is easy for us to illustrate the very newness of our thinking in the emotional sphere. In the early 1940's diagnosis was confined largely to symptomatic description. People were described as having an anxiety state, or as being depressed, or as being phobic. There were many, however, who were involved in the area of "nervous" disease who felt that this level of description did not furnish pointed enough information insofar as the individual himself was concerned. Those practitioners who wished to go beyond symptomatic description developed a two-fold diagnostic framework, not only giving a description of the person's symptoms but, in order to give more meaning to this diagnosis, they provided a description of the person's characteristic ways of dealing with his social environment. For example, they say an anxiety reaction in a basically obsessive-compulsive personality structure, or a phobic reaction in a passive dependent individual. This two-level approach, at the level of the symptom, and at the level of personality, renders the total diagnosis much more meaningful and points up our increasing efforts to try to understand a person as a person, and not as an isolated symptom. It is interesting to note that it was not until early in the 1950's that a new psychiatric code book was issued which takes into account this point of departure.

Now to what I consider the most important and most fundamental principle of all. Simply stated it is, every person always makes the best possible adjustment he can, in view of his personality make-up and in view of the situation in which he finds himself. This is not to say that an individual's "solution" to his situation is an adequate one, and indeed it may even be a painful one. But nevertheless if we were to see things through the person's eyes, we would find that he effects the best solution available to him at the time, again in view of his personality organization, and in view of his situation. The man who becomes depressed for no reason that he knows, the man who suffers with vague abdominal pains which defy medical intervention, the woman who drinks excessively, the man who is afraid to leave his home for fear something will happen, even the woman in left field chasing butterflies,—all of these people are making the best possible adjustment that is available to them. These solutions may be painful, certainly they are inappropriate and inadequate, but they are the best these people can effect. It might be well to say that, in a nutshell, one of the main tasks in psychiatry and psychology is to help these individuals to effect solutions that are more appropriate and more comfortable to them and to those around them.

It is crucially important that people who deal with people become more sensitized to, and aware of the various manifestations of emotional stress. It is oftentimes too easy to "beat" a person for his symptoms, or to become too involved in his symptoms. On the other hand the tendency to minimize a person's symptoms may leave him with the feeling that he is being misunderstood and ignored. There is a balance between ignoring

the presenting symptoms on the one hand, and the tendency to dignify them on the other. One must try to understand what motivates an individual to behave as he does and try to understand what he means, which does not always coincide with what he says. This attitude has been described as being able to feel with the patient, to empathize with him, to see things as he sees them, and, by Theodore Reik, "as listening with the third ear."

In a preventive approach mental health takes an increasing position of importance. Theoretically we do not wait until the "machinery" breaks down before we do something about it, but we try to recognize symptoms early and attempt to abort serious difficulties before they ensue. Even more ideally we hope to impart a point of view to the patient, in which he will take more and more responsibility for his own self-maintenance.

There is not time to discuss more than briefly two notions which are pertinent to industrial environments.

Absenteeism is regarded as a major problem from the points of view of both management and the industrial physician. Absenteeism is reported to cost industry in the neighborhood of 10 billion dollars a year, according to public health surveys. It is true that this is a staggering figure, but this is not, I believe, the major cost to industry. A far greater problem is the man who is only partially present, the man who works at 63% efficiency day after day. This is the man who gets along, not on "all eight cylinders," but perhaps "on five." This is an insidious problem because to all outward appearances this man is functioning well enough, and while his performance is off, he is not sufficiently ill that some configuration may be pinpointed. The tendency is to overlook. It is too easy to say, "he is just worried," or "he will snap out of it," or "he needs to take a few days off."

Industrialists and some industrial physicians, as well, have tended to play ostrich with these kinds of problems, instead of recognizing the inefficiencies as symptoms, and doing something about them. Instead, the tendency is to allow the problems to get really "full blown" to the place that drastic action is required. Of course, an obvious illustration is the problem drinker.

To put it more pointedly, I would suggest that the industrial physician is not insensitive to the "symptoms," but that he tends to ignore them because they have not as yet reached disturbing proportions. There are even a few industrial physicians who rule out emotional adjustment as a part of their legitimate interest, and who focus primarily upon the physical status of their charges. In my own section of the country it is not uncommon to hear, "there is nothing wrong with you but your nerves," implying to the patient that he is not to be bothersome because there is no identifiable organic disease. His nerves are his own concern and his own responsibility. Consequently, there are many people who suffer needlessly who could be helped, and who have been made to feel that they have a cross to bear all alone. Often this reflects an attitude of hopelessness and helplessness. The industrial physician is not reticent to ask for the help of the radiologist, the orthopedist, or the dermatologist, but he tends to shy away from the psychiatrist and the clinical psychologist.

The problem is not a simple one. There are many prejudicial problems to overcome that muddy the water. But if prevention is a goal, then the area of mental health must be invaded and not avoided. Often management itself is a major stumbling block and the task becomes one of education and orientation. To recapitulate, the matter of absenteeism is a serious one in most industrial environments. I entitle this problem as absences, real and apparent. The main point made is that the man operating at a level of efficiency far below his optimum, is much more a problem than the actual absentee.

Finally, there is one other area I would like to discuss and which I have labeled as, "keeping the peace." This, too, is a very insidious problem because of the emphasis in our culture upon being "nice" and "upon doing the right thing." Many companies try to impart the fiction that "we are one big happy family." From my own experience, if there is one single factor responsible for more unhappiness and for more emotional stress than any other, it is this "keeping the peace." For to keep the peace means that a man does what he thinks is expected, rather than as he would like to do or say. So there be no misunderstanding, it is necessary to men-

tion that it is not advocated that a person behave without control or without regard to consequence. This is the other extreme and equally a manifestation of maladjustment. I am talking about the "good boy," the person who bends over backward to please others and who lets his own wishes go by the wayside while he attempts to win favor. Many of the individuals suffering with vague physical complaints which are difficult to substantiate, are these "anxious to please everybody" persons. This is often the man who is hard to know because he guards his true feelings so avidly. This is the individual who may have "temper-tantrum-like" outbursts when the "indignities" become too much to bear.

It is important that we recognize him and identify him, because it is so easy to overlook him. He causes very little actual trouble because of his emphasis upon conformity. To all outward, casual appearances he is well-functioning. He may appear only briefly at the medical department for something, perhaps, to ease his indigestion. He is unobtrusive and he does not want to cause trouble. Yet this is the kind of "stuff" out of which many emotional disturbances are made.

The main reason for presenting this brief and incomplete vignette is to demonstrate that this, and presumably most other broad categories of individual behavior, must be evaluated qualitatively as well as quantitatively. What may be considered as desirable and "normal" may actually be harmful, where the individual himself is concerned. In general, when a person behaves one way, while feeling another, he experiences emotional discomfort. In fact, the well-adjusted person is often described as one who behaves as he feels, within the expectations of society. As a first approximation, the greater the "distance," or the lack of congruity, between these two modalities (behaving and feeling) the greater the emotional stress.

I have touched briefly upon several areas which are important to me toward the understanding of people and what makes them "tick." I realize that I have not been too specific in many of my remarks. However, my main attempt is to impart a point of view and an approach in dealing with essentially well people, people who are, at least, well enough to maintain regular jobs and who are, at least, minimally effective in their day-to-day efforts in living. I hope I have done this.

Anesthesia for the Aged:

A Comparative Evaluation*

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The authors believe their experiences favor the use of a general anesthesia in the aged when operations on the hip are contemplated.

THE PROBLEM OF THE MANAGEMENT OF ANESTHESIA for the geriatric patient has been a controversial one for many years, with vocal advocates of both general and conduction anesthesia as the method of choice.[1-3] Our interest in this subject of anesthesia for the geriatric patient undergoing surgery of the hip arose when there were two deaths from acute myocardial infarction in the immediate postoperative period in patients who had had spinal anesthesia. It was thought a study on the relative safety of spinal versus general anesthesia in the aged patient undergoing an operation on the hip might throw some light on one facet of the total picture of geriatric anesthesia. Selection of patients in a circumscribed age group, undergoing a standardized type of operation on one area of the body, and utilizing well-defined technics of anesthesia, appeared to be the most satisfactory method of eliminating the majority of variables that plague any controlled clinical study.

Method

This survey includes all staff patients, 70 years of age or older, who consecutively underwent operation for the placement of an Eicher prosthesis, an Austin-Moore pin, a Smith-Peterson nail or a Jewett nail at Jackson Memorial Hospital in the period September 1, 1957, to August 1, 1958. Included were both scheduled and emergency cases. The rating of the anesthetic risk of each patient was completed by the physician administering the anesthetic. All the anesthetics were administered by a resident in anesthesiology. Random selection of patients was accomplished by having the type of anesthetic each patient received determined solely by hospital number. All patients with an even hospital number were given a general anesthetic. If the hospital number was odd, a spinal anesthetic was administered. This rotation was strictly followed regardless of theoretical or practical contraindications being present for that or any type of anesthetic. Standard preoperative medication of 0.4 mg. of atropine was given to each patient in both groups.

The protocol followed for those patients who received spinal anesthesia was as follows. An intravenous infusion of 5% dextrose in water via a No. 18 gauge needle was started in the arm before the spinal anesthesia was given. The patient was left on the litter on which he was brought to the operating room; 10 inch blocks were placed under both wheels at the foot of the litter. The patient was then placed on his side with the injured hip up. The spinal puncture was performed between L. 4 and 5 with a No. 22 spinal needle. Light Nupercaine 6.6 mg. (10 cc. of Howard Jones' solution) was given into the subarachnoid space. Methedrine 20 mg. was given intramuscularly into the back immediately following this. The patient then remained in position on his side for at least 7 minutes. The level of anesthesia, as shown by response to pin-prick, was then determined before he was moved to and placed in position on the operating table.

The procedure followed for the patients who received general anesthesia was as follows. Induction of anesthesia was with a minimal intravenous dose of thiopental followed by 40 mg. of succinylcholine. The

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patient was then given oxygen and the glottis was sprayed with a 4% solution of cocaine. Oral intubation with an appropriately-sized Portex endotracheal tube was carried out under direct vision. The cuff was inflated. Immediately after intubation a 0.1% intravenous drip (1 mg. per cc.) of succinylcholine was started. Ventilation was controlled from the onset with a Jefferson Ventilator at 18 and 20 cycles per minute with 10 mm. positive and 5 mm. negative pressure. The anesthetic mixture used was nitrous oxide-oxygen at a flow rate of 5:2 liters per minute in a semiclosed system. The succinylcholine drip was given at the slowest possible rate consistent with controlling the ventilation. The drip was titrated by periodically slowing it until the patient showed some movement or initiated an inspiratory effort. Thiopental was used as sparingly as possible after the induction dose. All patients had had the tube removed and were breathing well on their own before they were removed from the operating table. The reason for utilizing this special technic of general anesthesia was to standardize the method, eliminating variables, as much as possible.

Results

This survey encompasses 90 operations, 46 done under spinal anesthesia and 44 done under general anesthesia. The relative equality in numbers in each group tends to substantiate the validity of our method of random selection of patients.

Table 1 lists some miscellaneous vital statistics observed in this study. Most of the patients were operated on as elective procedures and were accordingly seen and interviewed the night before operation. The few patients operated on as emergencies were seen immediately upon admission to the hospital, and were likewise carefully evaluated as to physical condition. This evaluation of existing complications was classified as to

TABLE 1

	Spinal	*General*
Age (Average)	78	79
Duration—from induction to completion of operation (Average)	114 min.	106 min.
Thiopental dosage (Average)	0	189 mg.
Succinylcholine dosage (Average)	0	395 mg.

TABLE 2

Preoperative Complications	*Spinal*	*General*
Circulatory	36 (78%)	35 (79%)
Neurologic	15 (32%)	15 (34%)
Respiratory	17 (37%)	21 (47%)
Gastrointestinal	4 (8%)	5 (11%)
Genitourinary	7 (15%)	11 (25%)
Metabolic	12 (26%)	15 (34%)

whether they were primarily circulatory, respiratory, neurologic, gastrointestinal, genitourinary or metabolic. Under this last category were included such diverse conditions as fever, obesity, recent weight loss, decubiti, hypovolemia and alcoholism.

Table 2 again emphasizes the comparability of the two series in the tabulation of existing preoperative complications.

The course of the two groups under anesthesia revealed some interesting differences. Of those done under general anesthesia only 2 (4.4%) patients required extraordinary attention. One (H.Z.) had a drop in blood pressure from 140/70 to 90/60 forty-five minutes after induction. This was believed to be due to surgical stimulation and was immediately corrected with 25 mg. of thiopental intravenously. The other patient (I.W.) had a sudden and complete loss of blood pressure with a palpable pulse 2 hours and 5 minutes after induction. This was corrected with a single small intravenous dose of Neo-Synephrine. Of the group given a hypobaric Nupercaine spinal anesthetic, 15 (33.3%) had an episode of hypotension requiring supportive therapy. An episode of hypotension was not treated pharmacologically unless the systolic pressure fell at least 40 mm. Hg. below control levels. The time of onset of this hypotension varied greatly in a range of 5 minutes to 2 hours and 40 minutes after the spinal anesthetic was administered. (Hypotension from blood loss was not considered to be a complication of the anesthetic.) Of this group 5 needed only a single injection of a vasopressor intravenously. This was 4 mg. of either Vasoxyl or Methedrine. The remaining 10 patients required a 0.001% Neo-Synephrine drip intravenously to sustain blood pressures at a satisfactory level. It was possible to discontinue all of these vasopressor infusions either in the operating room or the recovery room; no patients needed this supportive therapy after they were returned to

their rooms. Nausea accompanied the onset of hypotension in a very large percentage of the cases, but this was easily controlled with oxygen by mask and the administration of the vasopressor. Sedation in the form of intravenous pentobarbital sodium was necessary in 7 patients because of marked apprehension. Meperidine was given intravenously to 2 patients because of complaints of pain at the operative site. In one patient it was necessary to administer a general anesthetic (thiopental and nitrous oxide) 2 hours and 20 minutes after the spinal anesthesia was given. Absence of anesthesia at the operative site was confirmed at this time. An immediate effective spinal anesthetic was obtained in every patient and in no patient was the anesthetic level, determined by pinprick, above T-8.

The immediate postoperative period in the recovery room was characterized by remarkably few complications in both groups. Nausea and vomiting were conspicuous by their absence. The patients operated upon under general anesthesia were awake and answering questions sensibly within 5 to 10 minutes after cessation of surgery. None of this group had any memory of what transpired after induction of anesthesia, although the majority were moving or grimacing often during surgery. The patients operated upon under general anesthesia complained immediately of pain at the operative site and usually needed a narcotic in the recovery room. Those in whom spinal anesthesia was used seldom needed analgesics in the recovery room due to the prolonged action of the Nupercaine. Patients were discharged from the recovery room as soon as it was determined that all vital signs were stable without supportive therapy.

All the patients in this series were closely followed postoperatively until they were discharged from the hospital. No attempt was made to follow their course after discharge.

Table 3 lists the incidence of either extension of an existing complication or development of fresh postoperative sequelae.

TABLE 3

Postoperative Complications	*Spinal*	*General*
Circulatory	6 (13%)	6 (13%)
Neurologic	10 (21%)	8 (18%)
Respiratory	6 (15%)	7 (15%)
Gastrointestinal	4 (8%)	1 (2%)
Genitourinary	7 (15%)	1 (2%)
Metabolic	7 (15%)	8 (18%)

There were 12 postoperative deaths in this series, giving a gross mortality figure of 13.3 per cent. Four of these deaths were in the group given spinal anesthesia (mortality rate of 8.0%) and the other 8 had been given a general anesthetic (mortality rate of 18%). A brief summary of the operative and postoperative courses of each follows:

Case 1. J. H., aged 70, was given general anesthesia; he was rated a poor risk preoperatively because of marked emphysema, congestive failure, questionable pneumonia, and Parkinson's disease; operative course benign; died 90 days postoperatively of multiple decubiti with septicemia.

Case 2. F. H., aged 90, was given general anesthesia. He was rated a poor risk because of rales bilaterally, productive cough, atrial fibrillation, mental confusion and a temperature of 101°; the operative course was benign, he died 30 days postoperatively from active tuberculosis and malnutrition.

Case 3. A. S., aged 95, was given a general anesthetic. He was rated a poor risk because of emphysema with cyanotic cast, atrial fibrillation and senility; the operative course was benign with no hypotensive episodes and he was out of bed and doing well when he suddenly died with an acute myocardial infarction on the seventh postoperative day.

Case 4. E. J., aged 83, was given a general anesthetic. He was rated a fair risk because of rales in bases bilaterally and neurologic residua from an old cerebrovascular accident. The operative course was benign; he was out of bed the next day. On the second postoperative day he had a fresh cerebrovascular accident. He died 7 days postoperatively with pneumonitis, congestive failure and electrolyte imbalance.

Case 5. R. B., aged 88, received a general anesthetic. He was rated a poor risk because of asthma, poorly compensated congestive heart failure, history of Stokes-Adams attacks for 5 years, and a temperature of 101°. His operative course was benign and he was out of bed first at 4 days, followed by a Stokes-Adams attack which led to his death in congestive failure 29 days later.

Case 6. M. D., aged 79, had a general anesthetic. She was rated a poor risk as she had lain at home on the floor, where she had fallen, for over 48 hours, and was markedly dehydrated and disoriented. She was operated on as an emergency procedure, the course of anesthesia being benign. She died suddenly one week postoperatively of an acute myocardial infarction after a good postoperative course.

Case 7. S. S., aged 79, had a general anesthetic. She had been rated only a fair risk because she was bedfast, disoriented, hypovolemic and had basilar rales. There was a transient drop in B.P. from 130/60 to 90/60 immediately after induction, which required no treatment. She died 6 days postoperatively of hypostatic pneumonia.

Case 8. J. B., aged 70, received a general anesthetic.

He was rated a good risk, and a 4½ hour surgical procedure was accompanied by an uneventful anesthetic course. He received 300 mg. of thiopental and 1,140 mg. of succinylcholine (0.06 mg./kilo/min. of succinylcholine). This patient was ventilating well, unassisted, immediately postoperatively. He died suddenly in the recovery room one hour postoperatively from a ventilatory insufficiency probably secondary to the use of succinylcholine. This is considered to be an anesthetic death.

Case 9. I. G., aged 85, had a spinal anesthetic. She had been rated a poor risk because of uncompensated congestive heart failure, uremia and clouded sensorium. She did well during operation, receiving Nembutal in a dosage of 50 mg. twice for restlessness. She expired 2 weeks postoperatively from massive bilateral pulmonary embolism after a benign period of recovery.

Case 10. J. R., aged 88, was given a spinal anesthetic and was rated a poor risk because of multiple decubitus, ulcer, chronic brain syndrome and pulmonary fibrosis. The patient had a benign operative course but expired 37 days postoperatively after a prolonged downhill course marked by pneumonitis, urinary tract infection, uremia and septicemia.

Case 11. C. L., aged 77, received a spinal anesthetic. He had been rated a poor risk because of chronic brain syndrome and malnutrition. He had a stable but moderately hypotensive course during the operation and became normotensive soon after admission to the recovery room. Postoperatively he was out of bed for brief periods, but declined rapidly with cardiovascular collapse of unknown etiology 8 days postoperatively.

Case 12. E. C., aged 75, had a spinal anesthetic, and had been rated a poor anesthetic risk because of uremia and extreme obesity. However, he did well under spinal anesthesia, but developed a severe urinary tract infection and died in uremia 10 days postoperatively.

Comment

With the exception of the mortality figures, the postoperative complications arising in each group were at relatively comparable levels. Close scrutiny of each of the deaths failed to disclose any causative relationship with the anesthetic technic employed, with the sole exception of the one patient who expired from ventilatory failure secondary to the use of a relaxant. Therefore, in spite of a definite difference in postoperative mortality figures, it is difficult to state any firm conclusions concerning anesthetic technic and postoperative sequelae.

However, certain observations that do not lend themselves to statistical analysis have created a strong clinical impression that light anesthesia or analgesia with associated paralysis as described in the protocol, provides a more satisfactory method of anesthetic management in the aged patient undergoing hip surgery. This philosophy does not necessarily apply to aged patients undergoing all types of operations, since, for example, our experience with the geriatric patient undergoing transurethral resection weighs heavily in favor of spinal analgesia. Although there were no objections by patients to spinal anesthesia, a rarity in this day and age, in at least three instances where a unilateral spinal anesthesia occurred, the patients complained bitterly of discomfort in the unanesthetized leg. Excessive apprehension frequently required sedatives in the form of a barbiturate or narcotic in the face of an unstable blood pressure. Several of the procedures were done with the patient in the prone position, which was considered very unsatisfactory for the patient under spinal anesthesia. Although surgical preference openly favored neither method, it was apparent that the longer time needed for induction of spinal anesthesia rankled in the surgical bosom. The only positive factor favoring spinal analgesia was the interval immediately postoperatively when no narcotics were required, a fortunate thing since many of these patients were being sustained on vasopressor infusions during this period.

On the other hand, those patients anesthetized with general anesthesia utilizing analgesia plus relaxants, as described in the protocol, appeared to have a much more stable clinical course during operation in terms of measurements of standard vital signs. Their general appearance was excellent. Naturally, the strict precautions essential to the safe use of relaxants must be observed. Particular emphasis must be placed on the immediate observation in the recovery room where the diminution or absence of painful surgical stimuli may allow for re-blockade of the neuromuscular junction, a situation which unfortunately occurred in our single anesthetic death.

It would be most unwise to deny that both anesthetic technics can be satisfactory in the management of this age group, most of whom are prohibitive surgical and anesthetic risks. The mortality associated with hip surgery, under the conditions of this investigation, appears to be most closely related to the preexisting disease, and anesthesia by either

technic is a minor etiologic factor in gross death figures. However, the character of the operative and immediate postoperative course of patients thus anesthetized under general anesthesia strongly suggests that analgesia plus relaxants offers the more satisfactory method.

Summary

1. A group of 90 geriatric patients who had hip surgery were chosen at random for a comparison of operative and postoperative mortality and morbidity. Spinal anesthesia was used in 46 and general anesthesia in 44.

2. It is suggested that general anesthesia, utilizing the technic of analgesia plus relaxants, as outlined in the protocol, is preferable to the use of hypobaric spinal anesthesia.

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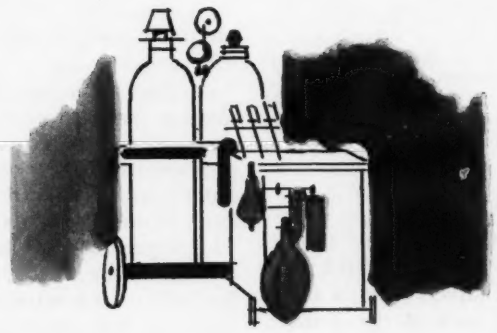

Preanesthetic Medication: 1958 Concepts*

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The authors have found that long tried methods of preanesthetic medication still seem to be the best.

THERE ARE FEW THINGS in medical practice which require as much individualization as does premedication; yet premedication is so often ordered empirically and routinely. Preanesthetic medication is actually part of the anesthetic. As such it should be prescribed by the individual who plans to administer the anesthetic. It should be selected on the basis of the general status of the patient, his psychic make-up, and the type of anesthetic to be used. Too often premedication is prescribed by individuals who are not directly concerned with the administration of the anesthetic and who have little concept of the purpose of the premedication.

Purposes of Premedication

The primary purpose of premedication is to provide psychic sedation. In other words, it is used to obtain a state of tranquility so the patient arrives in the operating room with a nonanxious and an indifferent air. Drugs are also given prior to anesthesia to reduce the activity of the mucous glands to avoid excessive secretions. Certain anesthetics have undesirable side actions which can be prevented by the administration of drugs prophylactically. Drugs are also given prior to operation to fortify impotent anesthetics. One may say, then, that there are four basic purposes for the administration of premedication: (1) for psychic sedation, (2) to minimize secretions, (3) for prophylaxis, and (4) to fortify impotent anesthetics.

The concepts of premedication have changed somewhat and, in some respects, are different from those of a quarter of a century ago. This is understandable because new drugs are now available for anesthesia and technics of using the old established drugs have been improved. One of the chief factors responsible for changes is that present-day anesthesia practice utilizes combinations of drugs where heretofore reliance was placed solely upon a single agent for a particular anesthetic. This presentation will describe these changed concepts.

Drugs Used for Psychic Sedation

Psychic sedation may be obtained by the use of one or a combination of several of numerous depressants of the central nervous system. Ever since the idea of premedication was conceived, reliance has been placed largely upon the narcotics. Claude Bernard[1] was instrumental in the adoption of morphine as a premedicant. Not long afterward the hypnotics were tried for the same purpose. Chloral was used by Forné and others to produce a state of tranquility. Later the belladonna alkaloids, atropine and scopolamine, were added to the morphine. Since that time there have been two schools of thought concerning the use of premedicants,—those who prefer the narcotics and those who prefer the hypnotics in basal narcotic doses. We find this division of thought has continued to exist into present-day practice. The early workers in the field of anesthesia soon learned that atropine was useful for its effect in suppressing salivation, and also noted that it tended to antagonize the effects of morphine. These facts, known for so long, are ignored by many clinicians even today. The combination of morphine and scopolamine is still widely used in present-day practice. It was also observed that scopolamine enhanced the effect of the narcotic and had a tranquilizing and amnesic action not possessed by morphine alone. As each new hypnotic and basal narcotic is introduced, it is tried for premedication or basal narcosis. The drug that

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did the most to popularize basal narcosis was tribomoethanol (Avertin) rectally. This produces a deep stupor accompanied by amnesia. This drug finally gave way to the intravenous barbiturates which are simpler to give and in many ways more effective.

Use of Narcotics. Another trend in premedication has been for certain groups of anesthetists to crusade against the use of the narcotics. They contend that the narcotics depress respiration, cause hypotension, nausea, vomiting and other untoward effects. Furthermore, the average preoperative patient is not in pain, they say, and therefore does not need a narcotic. They contend that barbiturates, such as 100 mg. pentobarbital or secobarbital, are as effective. The result of the admonitions of these workers has added additional confusion.

What about the narcotics? Should they be cast aside? Despite the objections of anesthesiologists, such as Beecher,[2] to the narcotics, they are still widely used for premedication. The argument that the preoperative patient undergoing elective surgery does not need a pain reliever is superfluous. It is true the patient is not in pain, but that is not the reason for using a narcotic. The pain relieving effect of a narcotic is obtained by elevating the pain threshold. This elevation of the pain threshold proves effective up to a given point of dosage. Beyond that point, there is no additional pain relief. The narcotic does, however, alter the psychologic response to the pain. In other words, the pain is there but the patient becomes indifferent to it, and does not care about it. The narcotic addict does not crave the drug because he is in pain. He craves it because it produces a feeling of well-being. In other words, a narcotic relieves anxiety and confers a feeling of well-being to a patient who is about to undergo an operation. It is this ability to relieve anxiety which makes narcotics useful for premedication. They relieve apprehension. The barbiturates are not nearly as effective in accomplishing this purpose, since they are, relatively speaking, mild in their action when used in hypnotic doses. When used intravenously, in basal narcotic doses, they are suitable for technics of anesthesia which utilize combinations, such as thiopental, nitrous oxide and succinylcholine. It is only when they produce a deep state of hypnosis, commonly referred to as basal narcosis, that the patient becomes indifferent, and develops amnesia. The relatively smaller oral doses which are recommended, do not accomplish this. The narcotics are far superior when inhalational anesthesia with a single agent such as ether or cyclopropane is used.

Objections to Narcotics. One cannot deny that the narcotics are frequently abused, and that excessive quantities are administered.[3] Too often they are used in patients who should not have them. Under these circumstances, depression of respiration and hypotensive states may result. One common error is to use average therapeutic doses in patients in the older age groups. Elderly patients are far less tolerant to depressants of the central nervous system. One-half to one-fourth the dose of a narcotic used for middle-aged patients is ample for the elderly. It is well established that hypotension may develop after the use of most depressants of the central nervous system, especially when the patient is subjected to abrupt postural changes. The narcotics, however, cannot be singled out among the depressants of the central nervous system as being the only ones having this property. Few of the depressants of the central nervous system are devoid of side actions. Antagonists such as nalorphine (Nalline) and levallorphan (Lorfan) are available to antagonize side effects of the narcotics. This is not the case with other drugs.

We obtain excellent results by using a combination of morphine and scopolamine. Ten milligrams of morphine combined with 0.4 mg. of scopolamine administered one and a half hours prior to anesthesia, in an average adult, produces an air of indifference, with amnesia, without circulatory and respiratory depression. The scopolamine enhances the cortical effects of morphine. Like atropine it antagonizes the depressant effect of morphine on the medullary centers. There is no comparison between the psychic sedation of the morphine-scopolamine mixture, and the widely used morphine-atropine combination. The synthetic narcotics, such as methadone, alphaprodine (Nisentil), and meperidine (Demerol) do not have the same intensity of action in relieving anxiety as does morphine. We use this combination as premedication for anesthesia using cyclopropane, ether, or the thiopental (Pentothal)-nitrous oxide technic.

Some anesthesiologists have become enthusiastic over the combination of morphine-scopolamine fortified with the ataractics of the phenothiazine series. The phenothiazine derivatives produce a summation when used with narcotics, so that the dose of narcotic may be reduced.[4] However, they are objectionable because they have serious side actions.

Use of Ataractics. The most recent concept concerning premedication centers about the ataractics or tranquilizers. Heretofore, little attention was directed to the primary site of action of central nervous system depressants. It was assumed they depressed from the cortex downward. Now it is well established that some act primarily on the cortex, while others act on areas below the cortex, such as the hypothalamus, and structures which control the emotions. Certain of the ataractics are capable of establishing emotional tranquility in disturbed patients. The only drug with a subcortical action used with the narcotic prior to the introduction of tranquilizers was scopolamine. The drugs being offered at the present time are numerous. As a result there is a good deal of confusion regarding which drugs are best to use. The tendency to drop the old for the new is all too prevalent in medicine. As each new drug with a depressant action is introduced, it is suggested that it be used for premedication. In order to be considered modern these days, one must cast aside the old and take on the new. As a result, there has been a wave of enthusiastic reports, with conclusions drawn from clinical impressions, which describe the use of drugs which have been only superficially studied.

Objections to Ataractics. The more potent of these, such as chlorpromazine (Thorazine), promazine (Sparine), proclorperazine (Compazine) and trifluprомazine (Vesprin) have serious side effects, most important of which is the sympatholytic action, which precipitates a difficult to reverse hypotensive state. It is true that many ambulatory psychiatric patients receive unusually large doses of phenothiazine derivatives without developing hypotension. However, when these patients are anesthetized, or undergo an operation, even under local anesthesia, they may develop hypotension of alarming proportions which is maintained for many hours and is very difficult to reverse. These hypotensive states have occurred following the use of single doses for preoperative sedation as well as in cases of prolonged administration. As a result, we are reluctant to anesthetize anyone who has had chlorpromazine or one of its allies of similar potency, within 48 hours of operation.

Promethazine (Phenergan) is the mildest of this group, and the one which manifests the least hypotension and side effects.[5] This drug was well established as an antihistaminic long before it was realized that it possessed a tranquilizing effect. However, mild hypotensive states have been reported by some workers when they have employed it preoperatively. We have not encountered any such responses.

The efficacy of promethazine used alone is not impressive. Promethazine used alone for sedation and amnesia is a weak and unpredictable sedative. Frequently it causes restlessness and mild excitement rather than tranquility. In combination with narcotics or barbiturates it does enhance their sedative action and permits use of similar doses. Our experience with it has been largely with children. In children there is a variability of response to all premedicants. In only one-third to one-half of the cases is sedation adequate and satisfactory. In the others, there is either under- or over-sedation. We hoped that the addition of promethazine to the narcotic would eliminate this variability of response. It does not, however, seem to accomplish this. Variability of response was as frequent with combinations of the promethazine and the narcotic as with the narcotic and scopolamine. With equivalent doses some patients still were awake and apprehensive while others were overly depressed. In adults we obtain satisfactory results by using a narcotic and scopolamine alone, using the same doses other workers use when they add a phenothiazine derivative to their mixture. We could see no point in adding a third drug which could possibly precipitate hypotension, when two well-established drugs are effective.

Use of Anticholinergic Drugs

Another aspect of premedication about which controversy exists is the use of antisecretory drugs. Some practitioners still op-

pose use of antisecretory drugs for premedication. However, these drugs are absolutely necessary, particularly when inhalational anesthetics are used, to prevent the secretion of mucus. From the time premedication was first suggested, atropine has been used for this purpose almost exclusively. Atropine is a racemic mixture of tropine tropate. Levo tropine tropate, known as levohyoscyamine (Bellafoline), is the active physiologic component of atropine. The dextro compound is physiologically inactive. Levohyoscyamine (or Bellafoline) is at least twice as effective in suppressing the secretions as atropine is in comparable doses. We[6] employ levohyoscyamine in preference to atropine. Scopolamine is equally as effective as levohyoscyamine in suppression of secretions. In addition, there are little or no changes in pulse rate when it is employed. Levohyoscyamine causes an average increase in pulse rate in adults of 25 per minute. Thus, scopolamine has a dual effect which makes it desirable as a premedicating agent. It enhances the tranquilizing and amnesic effect of the narcotic with which it is used, and it produces the necessary drying effect. In addition it overcomes a tendency to nausea. The synthetic anticholinergic drugs, such as oxyphenonlum bromide (Antrenyl), methantheline bromide (Banthine), and dibuline sulfate have, in our experience, been less effective and desirable than scopolamine and levohyoscyamine. Side actions, such as extreme tachycardia or hypothermia, have been encountered when doses necessary to suppress secretions were used. These synthetic anticholinergic substances have been introduced by the manufacturers as spasmolytic drugs for gastrointestinal spasm. In most cases manufacturers claim that these drugs are devoid of antisecretory effects, since this would be an undesirable side action in a drug prescribed for this purpose. Thus, the majority of them are not intended for suppressing secretions.

The most important and frequent side action caused by anesthetics, for which premedication is used prophylactically, is vagal excitation. Such excitation is noted most frequently when the halogenated hydrocarbons, such as ethyl chloride, trichlorethylene, and the recently added fluothane are used for inhalation anesthesia. Vagal effects of less serious importance occur with cyclopropane. Vagal excitation sometimes occurs reflexly from mechanical stimulation during operation. Here again atropine is the standard agent for suppressing vagal activity. The writers find levohyoscyamine to be more effective because it has a greater vagolytic action than atropine. Scopolamine is not as effective as atropine or levohyoscyamine as a vagolytic drug, particularly in the cardiac portion of the vagus.

The anticholinergic drugs are also used for premedication in patients who are to receive thiopental (Pentothal) to prevent laryngeal spasm. Their value for this purpose is doubtful. The vocal cords are composed of striated muscle and are, therefore, not affected by atropine and other anticholinergic drugs. It is a well-established fact that the muscle relaxants are far more effective in suppressing laryngeal spasm. However, the use of anticholinergic drugs with thiobarbiturates, such as Pentothal and Surital does have some merit because it may reduce the possibility of bronchial spasm, since bronchiolar tone and activity are under control of the vagi.

Decrease of Amount of Anesthetic Required

Claude Bernard and early workers who pioneered in the field of premedication noted that induction of anesthesia was smoother when drugs were given before anesthesia and that less ether or chloroform was required to accomplish their purpose. Since this observation was reported there has been a division of opinion as to whether or not less anesthetic is necessary when premedicants are added. There is experimental data to support both contentions. There are those who have attempted to prove, by laboratory studies and otherwise, that premedication influences the quantity of drug necessary for anesthesia very little.[7] Anyone with any clinical experience in anesthesia knows that it is much simpler to anesthetize a patient who has had premedication with morphine than one who has had a hypnotic dose of a barbiturate or no premedication. Whether or not laboratory data support the fact that there is an additive effect between impotent anesthetics and the premedicant is immaterial. From a clinical standpoint, it is almost impossible to induce satisfactory anesthesia without premedication. Besides, smaller concentrations of

nitrous oxide are then necessary to maintain anesthesia. Perhaps the additive effect is of little consequence when the more potent agents, such as ether or cyclopropane are used. Few will dispute the fact that impotent gases, such as nitrous oxide or ethylene are best administered in combination with potent premedication agents.

Summary

Premedication should be considered as part of the anesthetic. Psychic sedation, antisecretory activity, fortification, and prophylaxis are the desired goals. In spite of a multitude of new drugs in anesthesia, the technic of premedication has changed very little from that of the earliest workers. The narcotic in combination with belladonna alkaloids remain versatile and reliable agents.

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Historical Development of Obstetric Education in the South*

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OBSTETRICS, both as an art and as a science, is difficult to consider from a geographically limited point of view, since its scope is international. In a sense, however, it is appropriate for us in this Section to review the development of obstetrics in the 16 southeastern states as a background for better understanding of the problems that face us in the present.

Medical education and service, two inseparable facets of our professional activity, have had "a glorious past, a drastic decline; they are now experiencing a promising present," and though they face serious problems, our hopes for a brilliant future seem well-founded.

Medical education in the South may be said to have begun in 1799 with the establishment of the medical school at Transylvania University in Lexington, Kentucky. This was only 34 years after John Morgan established the first medical school in Philadelphia. During the next century, 75 schools were organized and flourished for a time, but by 1940 all but 16 of these had been closed.[1]

Many of the medical schools founded during the nineteenth century in both the North and South were commercial ventures for the collection of fees from students, often with the additional motive of augmenting the teachers' practices by referral of patients. These schools were "lecture mills" in which the same course would be repeated each year; there was little or no practical work except that provided by apprenticeship to an older physician. "Sessions at most institutions were limited to 3 or 4 months, since most of the students were already practicing and could not afford to desert their patients for a longer period of time. Although the course usually lasted for two sessions, there was no division in the grades; the pupils sat through the same curriculum twice over on the theory that what they did not understand the first time they might understand the second."[1] One of the southern schools was in operation for 27 years before there were any hospitals in its vicinity. In fact, as late as 1894 Osler stated that his greatest contribution to medical education was "bringing the students to the wards."

There was, however, a single honorable exception to the general deficiency of clinical teaching in the South. The 1834 prospectus of the Medical College of Louisiana (now Tulane University School of Medicine) carried this statement: "New Orleans was selected for the location of the school because its hospitals are the largest in the Southern and Western states, and because its hospitals are filled with patients so that Practical Medicine and Surgery can be taught at the bedside of the patient, the only place for this study; and because many surgical accidents occur, and it is consequently the best field for the study of Surgery in the Southwest."[1] Among the distinguished obstetricians on its faculty were Dr. Francois Prevost who, in 1830, performed the first cesarean section in America.[2] Dr. Dubourg, an old surgeon of the imperial guard of Napoleon who practiced in New Orleans in the 1830 era, was a pioneer in the performance of vaginal hysterectomy in this country.

A premedical curriculum consisting of "adeptness in Latin, Greek, French, Mathematics, and Natural Philosophy" was recommended by John Morgan in 1765, and in 1820 Daniel Drake insisted that "every pupil should have a first class education in Literature, Classics, French, Mathematics, Mechanics, History and Geography."[2] However, these premedical requirements were abandoned until the founders of Johns Hopkins University restored a reasonable academic standard for the entering medical student.

The second important medical center of

*Chairman's Address, read before the Section on Obstetrics, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

the South was developed in Baltimore, where the College of Medicine of Maryland was organized by Dr. John B. Davidge in 1807.[2] In 1813 this institution became the Medical School of the University of Maryland.

In 1878, Dr. William H. Welch organized the Johns Hopkins Medical School, established in 1893. Its long and distinguished history includes the careers of J. Whitridge Williams, Howard Kelly, T. S. Cullen, and others who made an indelible impression as medical educators in obstetrics and gynecology.

The state of Georgia deserves credit for early recognition of the necessity for improved teaching methods in the medical school.[3] There, Antony and Dugas, both of whom had served apprenticeships under excellent practitioners and had taken courses of study in northern institutions, realized that medical training was inadequate and they were the first to propose the extension of the time of study from 4 to 6 months. They were also insistent that the standardization of medical education and practice would never be achieved until an appropriate national accrediting agency was in operation.

In 1837, Dr. P. F. Eve, who had recently returned from Paris, proposed in the Southern Medical and Surgical Journal the founding of a National College of Medicine patterned after the French system.[3] This College was to set the standards of training and determine the requisites for the degree of Doctor of Medicine. The logic of this suggestion is apparent from the fact that most of the existing schools, while partially supported by public funds, were in fact private institutions whose chairs were filled by busy practicing physicians. In 1838, the faculty of the University of Georgia School of Medicine announced that the professors of Anatomy and Chemistry, respectively, were to devote their full time to their professorships, and that the two terms required for a degree had been lengthened from 4 to 6 months.[3] Jealousy and competition for the fees of students kept the larger institutions from adopting the lengthened course and from sponsoring the formation of an accrediting association. Even as late as 1846, Dugas thought it necessary to publish a defense of the action of Dr. Nathan Smith Davis in forming the American Medical Association.[3] Shortly after this, Georgia contributed her share to the advancement of medical education by continuing to send delegates to the American Medical Association conventions throughout the time the medical colleges had specific representation. In 1852, the American Medical Association changed its policy in a resolution that altered the constitution to admit delegates from county and state societies, following a lively discussion as to whether the interests of 30,000 practitioners should suffer in order to cater to those of 200 professors. "Throughout the formative years, Georgia's requirements for a degree were more stringent than those generally stipulated by the American Medical Association, even as late as 1858. One term only was adopted, although clinical instruction in a hospital was necessary for licensure."[3]

The next critical change in the philosophy of medical education is made clear by the following statement of the Dean of the Medical School of Georgia as published in the annual announcement for 1890-1891: "We are watching the present efforts on the part of many Medical Colleges and Boards of Health throughout the country, towards reform in the schools, and an elevation of the standards of medical education with deep interest but many misgivings as to the attainment of any practical result. We have experimented much in the same direction, both independently and in cooperation with other colleges, but hitherto with very partial success. We are quite sure that such results will not be attained by the adoption of any set of arbitrary rules, regulations and requirements.

"We cannot require of our students what they have no means of obtaining. . . .

"The lack of education among our people is therefore in a large measure due to their poverty. It should not be forgotten that only 25 years ago this people was subjected to an act of military spoliation, unparalled in history, which left them little besides land upon which they stood. Experience teaches that our students cannot on the average well afford the time and money necessary for the present three years' study in medicine with the required preliminary training."[3]

By 1890 the early illustrious figures in Southern medicine had grown to be old men. A period of decline was inevitable, since economic depression and deficiency of educational facilities had prevented their replace-

ment by younger men of comparable caliber. The better students of the region customarily sought their medical education in non-southern schools, and many of them failed to return to the South following graduation.

In 1901, there were 159 medical schools in operation in the United States.[4] In these institutions, 26,417 students were enrolled, and 5,444 of them received medical degrees in that year. This state of affairs continued to prevail, and explains the attitude of Dr. Henry S. Pritchett of the Carnegie Foundation, who, in 1910, wrote of "an enormous over-production of uneducated and ill-trained medical practitioners."[4]

November 19, 1908, is an important date in the history of medical education in America. On that date the trustees of the Carnegie Foundation authorized a study and a report upon the medical schools in the United States, and appropriated the money necessary for this undertaking. Under the direction of Abraham Flexner, this committee presented their history-making comprehensive report on all the medical schools in the United States and Canada, the famous "Flexner Report."[4] In the course of their travels, the members of the Committee encountered hostility and resentment on the part of many of the 150 schools visited, which took the unfortunate position that they were private institutions and the public was entitled to know only as much as the schools were disposed to communicate to them. In spite of the opposition of these institutions there were strong forces both within and outside the medical profession operating to improve matters. Flexner[4] himself made a point of commending the Council on Medical Education of the American Medical Association and the Association of American Colleges. As a direct result of the Flexner Report, several colleges discontinued their medical department altogether, while in other instances large sums of money were raised to improve existing standards of medical education. Large foundations generously supported the cause of education, and the leaders of the great universities followed it. The extensive alterations in medical education between 1900 and 1950 were caused partly by the rapidity and extent of the change in medicine itself and in general science, partly because of the changes in the social and economic background of medicine, and partly because of the changes in the field of education. These 50 years have seen great growth in population and its expanding industry and wealth, participation in two great wars, and many other influences that have played their part in altering the problems of medical education and the methods of meeting these problems.

The Place of Obstetrics in the Medical Curriculum

Originally obstetrics was not a major topic in the curriculum of universities. As a matter of fact, the earliest obstetricians were not men.[5] For 13 centuries the physician was not allowed to attend normal deliveries, although in the seventeenth century they began to participate to some extent. The predominance of male obstetric attendants was not evident until the middle of the nineteenth century.

Preventive obstetrics is considered an American contribution to medicine, as it was in this country that prenatal care was first systematically practiced.[5] Although John William Ballantyne, who graduated at Edinburgh in 1883, pioneered in advocating routine prenatal care, it remained for the Boston Nursing Profession to introduce a comprehensive prenatal program (in 1901). Even before Ballantyne's time, a pioneer woman physician, Dr. Mary Jackson Whitney of Rochester, Minnesota, had published the following notice in the Rochester newspaper:[5] "Ladies, if you intend to secure services of Dr. Whitney during your confinement engage her at your earliest convenience. Twenty years experience as midwife causes her to prefer visiting her patients before the event as well as after, in order to render the occasion comfortable and safe. Her subsequent visits are to insure as far as possible perfect health combined with an elegant figure. No extra charge for advice."[5] To the present, the importance of properly conducted prenatal care has continued to be appreciated, and its consistent utilization in the care of the obstetric patient has been significant in reducing preventable fetal and maternal mortality.

With the organization of the American Board of Obstetrics and Gynecology in 1930, American obstetrics attained full stature as a bona fide specialty. The concept of the combined specialty was developed following the recommendations of such leaders as Findley,[6] who early advised the unification of departments of obstetrics and gynecology in medical

schools and the staffing of those departments by qualified specialists in obstetrics and gynecology. An adequate departmental training program, as outlined by him, including pathology courses, manikin demonstrations and clinical clerkships, was subsequently adopted by accredited schools. In addition to the medical schools' responsibilities for undergraduate instruction, their duties to the graduate physician have been stressed in recent years. Holmes[7] was among the earliest authorities to recommend that teaching institutions provide adequate postgraduate courses in obstetrics, suggesting that state universities develop courses of the "circuit" type for local practitioners so they might improve their methods and keep up to date with modern developments. At the same time, Ehrenfest[8] warned against the abuse of newly developed analgesic and anesthetic methods which might unnecessarily jeopardize both mother and baby; he became an outspoken opponent of nonindicated interference. Ehrenfest also suggested appropriate changes in birth and death certificates so more complete and precise information could be obtained from them. The problems of obstetric nursing education were investigated in 1920 by a Committee headed by Kosmak;[9] their recommendations advanced the cause of good obstetrics by pointing out effective ways in which to prepare and control maternity nursing personnel. Cooke[10] and others have stressed the pressing need for better methods in the teaching of obstetrics, and have outlined ways in which improvement might be attained. Commenting on maternal and fetal mortality in the United States, Stander[11] wrote: "I go so far as to say that the blame for the number of maternal and fetal deaths recorded annually in this country should be ascribed, in great part, to the deans and curriculum committees of our medical schools." The same author was of the opinion that obstetrics has been given a place in our universities which is subsidiary in importance to general surgery and internal medicine, even though it is clearly a medical discipline of comparable clinical value.[12] In a similar vein, Bartholomew[13] has stated that the part played by the medical profession in the prevention of maternal mortality is inseparably linked with the teaching of obstetrics in our medical schools.

As the result of the influences exerted by the authors quoted, and others of comparable eminence, Litzenberg[14] was able to state in 1938, "I believe we can safely assert that the teaching of obstetrics in medical schools is steadily improving, and that more schools are giving adequate instruction." Side by side with the education of the physician, the necessity for education of the public, and particularly of expectant mothers, has become apparent in recent years. The universities have not yet assumed their full responsibilities in the total field of obstetric education, although increasing awareness of their deficiency in this regard may ultimately further improve this situation.

Obstetrics in the Southern Medical Association

On November 15, 1920, at the Watterson Hotel in Louisville, during the fourteenth annual meeting of the Southern Medical Association, a committee was appointed to draw up resolutions for the formation of a Section on Obstetrics to be presented at that meeting. At that time, there were 8 previously established sections of the Southern Medical Association. At the 1920 meeting, obstetrics, radiology, and orthopedics and traumatic surgery were added. Since that date, 9 other sections have been established. The report of the Resolutions Committee was adopted, and the committee was instructed to present the resolutions to the Council at the current session. A nominating committee placed before the section the names of Dr. Calvin R. Hannah, Dallas, Chairman; Dr. J. T. Altman, Nashville, Vice-Chairman; and Dr. James Garber of Birmingham, Secretary.

In the years that followed, stimulation in the thinking of obstetrics and obstetric teaching was manifested by such titles of papers as, "The Ideal Obstetrician," "The Training of an Obstetrician," and "Progress in Obstetrics." At the third meeting following establishment of the Section, the first statistical review of fatalities in obstetrics was presented by Dr. George Dempsy of the Registration Bureau of Vital Statistics of the State Board in Louisiana. At the next meeting (the eighteenth of the Southern Medical Association), the Chairman's Address was, "Prenatal Care in the South" by Dr. Edward Speidel. At the nineteenth meeting in Dallas in 1925, the Chairman's Address was entitled, "Diagnosis in Obstetrics." At this meeting a discussion of low cervical section with motion pictures evoked quite a lively discussion. At this time,

the Section encountered difficulties in equitable proportion of program time. The Section on Gynecology originated in 1928 in Asheville, and the first gynecology program was presented at that meeting. The Chairman's Address of the obstetrical section by Dr. W. T. McConnell was, "Internal Podalic Version." On this same program was a paper on "blood transfusions." At the twenty-third meeting in 1929, at Miami, the Chairman's Address was, "Prevention of Congenital Syphilis." There was also a symposium on eclampsia. A symposium on maternal welfare was a feature of the twenty-fourth meeting. At the 25th meeting in New Orleans, in 1931, a joint session with the Section on Gynecology was included for the first time. The first paper on the Aschheim-Zondek pregnancy tests to be read before the Southern Medical Association was presented at this meeting. It was at the twenty-eighth meeting, in San Antonio, that a member of the Section was appointed to represent the Section on the American Committee on Maternal Welfare. At the twenty-ninth meeting in St. Louis, the then topical subject on, "Total Against Sub-total Hysterectomy" was discussed by Drs. Hagman and Crossen.

At the Cincinnati meeting, in 1943, the scope of the program was necessarily restricted by the prevailing wartime conditions. Social activities were considerably curtailed, and on the program formal clinical sessions were omitted and this allotted time given to sections. Chairman R. A. White presented a paper on, "Puerperal Sepsis, Treatment With Penicillin," an early case report on this subject. At the forty-first meeting in Baltimore, 1947, the Chairman's Address focused attention on Maternal Morbidity and Mortality in the South by presenting an analysis of 175 deaths in North Carolina.[15] By now there had been a gradual increase in the number of scientific exhibits and their quality had greatly improved. At the forty-fourth meeting in Dallas, Chairman Ruch presented a timely discussion on obstetric practice under conditions imposed by all out warfare, including an outline of possible disaster plans, as well as the obstetric implications of thermal and radiation injuries. In 1956, at the Fiftieth Anniversary meeting in Washington, D. C., an excellent program was presented. In keeping with the turning point represented by the Golden Anniversary of the Southern Medical Association, Dr. Garth Jarvis,[16] the Section Chairman, presented an address appropriately entitled, "The Past, the Present, the Future."

One of the first attempts at obtaining statistical data on maternal deaths was that by Dr. George W. Kosmak in 1917 in New York City.[17] It was not until 10 years later that sufficiently accurate data for evaluation was obtained.

Dr. Watson[17] states that, "I cannot but believe that the 40% reduction in maternal mortality between 1933 and 1940 was a direct outcome of that report together with the 'fifteen states' study' and of the Philadelphia group with which the name of Dr. Phillip F. Williams will always be associated." The improvement was ascribable to improved medical methods as well as to the realization of the importance of preventive medicine on the part of both physician and patient.

During these years up to 1940 the reduction in the number of deaths from sepsis had not kept pace with that due to the other causes above mentioned. It was about 1940 that the sulfonamides and shortly thereafter that penicillin and other antibiotics became generally available. From then on the death rate from sepsis began to fall even more rapidly than that from other causes so that in 1950 the total maternal mortality in the United States was only 8.3 per 10,000 live births, truly a striking contrast to the 67.3 of 30 years previously. The maternal mortality rate for 1956 was 3.8 deaths per 10,000 live births. This is a 76% reduction during the preceding 10 years.

Prior to 1915 there was no so-called registration area, established by the Census Bureau. Statistical material has become progressively more accurate and inclusive as the years have passed since 1900. It is logical that death reports should be the first to accumulate at a national level and these are of some value as far back as 1900.[12] The registration area was started in 1915 with ten states and the District of Columbia. Birth and death reports are not given for the continental United States until 1933. From 1915 to 1932 this area was an expanding one and certain estimates were made to show the national picture. During this time certain procedures had been changed, and thus the data from year to year had to be adjusted according to certain set rules regarding live births, still-births, death, and their causes, thereby affecting the rela-

tive frequency in certain categories. Many deficiencies still exist in the functioning of the maternal mortality committees. When the statistics of the Census Bureau revealed a true picture of obstetric mortality, suspicion turned to conviction that child-bearing was followed by too many deaths and too much morbidity and that something must be done about it.[12] In 1920, the Census Report revealed a sorry picture; 15,000 mothers were dying every year to say nothing of the sad trail of morbidity. More than 75,000 babies were born alive, but died before they were a month old, and another 80,000 were stillborn. These 160,000 mothers and babies, not including the 70,000 estimated abortions, slowly aroused professional and lay opinion to the realization that the obstetric practice in the early 1920's was at a low ebb.[12] This conviction was further strengthened when subsequent investigation revealed that more than half of the deaths were preventable. How could this prevention be accomplished? —first, by better undergraduate teaching; second, by education of the public, and particularly of expectant mothers; and third, by postgraduate education of the physician during the years of practice.[12]

In 1918, The Committee on Maternal Welfare was formed. This was exclusively a medical organization that developed most of the plans which were to lower our high mortality rates.[18] This conference was succeeded by the Conference on Child Health and Protection. Ideas later developed for this White House Conference had been originally developed by the Joint Committee on Maternal Welfare. This Committee was incorporated in 1934, and in December of 1956, its name was changed to The American Association on Maternal and Infant Health. The purpose of this new organization was to implement ideas formulated at the White House Conference and enlarge them as time and knowledge indicated. One of the important developments of the American Committee was the inauguration of the American Congress on Obstetrics and Gynecology, the first of which was held in 1939 in Cleveland. There have now been six American Congresses. They serve to bring together professional groups who are interested in improving maternal and child care.

Over the country as a whole, however, progress of which we are now capable is often impeded because available knowledge is not put to practical use. Committees appointed by both state and local medical societies have reported many factors involved in maternal deaths. These reports have been illuminating. Statistical analysis of maternal and fetal morbidity and mortality should be continued in every area.

A continuing education must be carried to the physician in general practice. Much necessary information can be disseminated through hospital staff meetings, county society meetings, refresher courses and formal postgraduate courses. When indicated, the so-called "circuit courses" may facilitate teaching in isolated areas. The potential of educational television is still beyond comprehension. Noncommercial education in television is now in the experimental stage. It can bring current knowledge directly from the medical school to the physician.

Education of the public and of the individual patient is of tremendous importance in the community. The patient should recognize the importance of prenatal care and should have enough basic knowledge so she may select her physician on merit. She should be able to evaluate accepted treatment procedures for common complications as well as signs of serious disease. The individuals who comprise a community should be aware of minimum requirements and hospital facilities.

Important information may be made available to all physicians, to all individuals and to society as a whole by the use of every medium of communication available.

According to Watson,[17] "In the year 1933, the maternal mortality rate in the United States was 61.9 per 10,000 live births. In the year 1950 it was 8.7 per 1,000 live births. Prior to 1930 the rate had not diminished but had rather shown a rising trend, 60.8 in 1915, 64.7 in 1925, and 67.3 in 1930."

Miller estimates that 60% of our present maternal deaths—5 per 10,000 live births—may be prevented.[18]

In the parlance of the football coach, "The last three yards are the most difficult to gain, and in order to score we must have a strong line, a hard-hitting backfield, and a brilliant quarterback."

If we are to prevent 60% of the maternal deaths occuring today we must think in terms

of teamwork, strenuous effort and an unfaltering spirit.

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CASE REPORT

Treatment of Meprobamate Intoxication with the Use of Methyl Phenidate: Case Report

DAVID POTYK, M.D., *Orlando, Fla.*

Since 1950, when meprobamate (2-methyl-2-N-propyl-1, 3-propanediol dicarbonate, — Miltown, Equanil) was introduced, it has been used for many conditions, primarily in anxiety states and for psychoneurotic disorders. There have been comparatively few toxic manifestations of this drug even in large overdoses. Primarily there appears to be drowsiness and sleepiness associated with overdosage; in a comparatively few cases there has been respiratory depression or cardiovascular collapse. The purpose of this paper is to discuss the treatment of cardiovascular depression and collapse, and respiratory depression following an overdosage of meprobamate in an elderly individual.

Case Report

A 71 year old white woman was brought to the Emergency Room one and one-half hours after the ingestion of 24, 100 mg. meprobamate tablets. At the time of the initial examination the patient was comatose, flaccid and in shock with a blood pressure of 50/0. Respirations were 12 per min. An intravenous solution of 5% dextrose in water was started immediately. She was given 1 cc. of mephentermine sulfate (Wyamine) intramuscularly and 100 mg. of methyl phenidate (Ritalin) intravenously and another 100 mg. was added to the intravenous solution.

The patient was hospitalized, placed in an oxygen tent and given another 1 cc. of the vasopressor. She remained flaccid with a blood pressure below 80 systolic during the next 12 hours. During this time the patient also had a marked drop in temperature, the rectal temperature falling to 93.8°. During the first 12 hours after admission, a total of 450 mg. of methyl phenidate was given intravenously as well as 3,500 cc. of fluids intravenously.

After the first 12 hours the patient began to stir, reflexes were hypoactive, respirations increased and the B. P. rose to approximately 100/60. The methyl phenidate was discontinued and at the end of 24 hours she was fully awake, moving and alert.

Summary

The case described was an attempt at suicide with meprobamate. Marked improvement followed treatment with the use of methyl phenidate intravenously and eventual recovery. It appears this drug may be a useful antidote to meprobamate intoxication and by itself has had few side reactions.

Florida Sanatarium and Hospital

Observations on 1,500 Patients: Rapid Mobilization of Patients Following Cerebrovascular Accident*

JOSEPHINE J. BUCHANAN, M.D.,† *Washington, D. C.*

PATIENTS ADMITTED to the District of Columbia General Hospital with a diagnosis of a first acute cerebrovascular accident are seen by the Physical Medicine and Rehabilitation Service within 24 hours of admission, as a part of the program of total care for the patient.

Unless severe complications supervene, the patient is started on tilt-table elevation, and arm and leg activities within an average of 3 days after admission. He is also started immediately on self-care with the good arm, range-of-motion and proprioceptive stimulative exercises, sling support of the involved arm, and speech stimulation.

As soon as the patient can tolerate the upright position on the tilt-table for 3 to 5 minutes, (usually within 2 to 3 days of starting it) his knee is splinted, if necessary, and he is placed within the parallel bars. As soon as ambulation in the bars is achieved, he is begun on independent ambulation with or without aids (crutches and canes).

As has been documented before, 88% of the patients so-treated achieve independent ambulation with an average stay in the hospital of 27.6 days.[1] Ability to walk independently is obviously measurable, and thus is used as the yardstick of the success of a treatment program for the hemiplegic due to cerebrovascular accident.

There are, however, other processes which are not so concretely or obviously measurable, but which, nonetheless, can be observed and should receive greater consideration. It is with the idea of challenging research in these areas that we are recording some observed processes in the patient having had a cerebrovascular accident, which we feel are the result of the early and vigorous reactivation program.

In this group of patients there have been no cases of hypostatic pneumonia, no thrombophlebitis, no decubitus ulcers, and rapid loss of incontinence. This is easy to understand since bedrest is not a part of the treatment program after the first three days.

Another change which we have observed in our patients is that there is rapid and complete clearing of the sensorium shortly after tilt-table elevation is begun. This occurs in a far greater number of patients and more rapidly than in those patients who are left at bedrest for several weeks. The exact mechanism of this is, of course, not understood, and points to the need for basic research into such possibilities as increased cerebral blood flow and metabolism, or whatever other process is at work.

One outstanding difference in our patients is the very few cases of continued speech impairment. We have been struck by the small number who have residual speech defects. We estimate these to be less than 1 per cent. Again we are forced to relate this to the effects of early activity. Or, conversely, to the effects of not continuing bedrest.

As a rule, the single greatest complaint of patients having had a cerebrovascular accident in their convalescent and chronic phases, is that of shoulder pain. As is well known by most family physicians, this complaint is all-consuming to the patient and gives the physician a most difficult symptom to treat. Once contracture and pain have become established in the shoulder, it is almost impossible to remove it by any treatment whatsoever. It is also well documented that contracture and pain in the shoulder occur with great rapidity and may be well established by the end of even one week of immobility. In our series of patients these conditions have been entirely eliminated. The range-of-motion exercises started the day of admission, and the support of the shoulder to prevent the gravity pull on the brachial plexus and joint capsule and ligaments have resulted in free shoulder joints and no pain. We have, by contrast, received

*Read before the Section on Physical Medicine and Rehabilitation, Southern Medical Association, Fifty-Second Annual Meeting, New Orleans, La., November 3-6, 1958.

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many patients, transferred from other hospitals, who are so troubled by shoulder pain that they cannot concentrate on efforts to walk. Therefore, exercise plus support, begun immediately after the onset of hemiplegia seem to be the factors in preventing shoulder pain.

Many physicians feel that early activity in the patient having had a cerebrovascular accident is contraindicated, since it might produce further extension of the damage or "trigger" a second such episode. In our 1,500 patients in their first attack, only one individual has suffered a second episode while undergoing the treatment program as conducted here. This covers the period of 27 days in the hospital, plus the average of 4 follow-up treatment periods as an out-patient. Again, here is an area for intensive research.

As a final component in the observation of our patients, a study was made by a 5 year follow-up of their ambulatory status. This study showed that 85% remained ambulatory over a 5 year period. Again, this needs comparison with other patients on different treatment regimens.

As is obvious, there are many areas of research interest in the problem of management of the patient having had a cerebrovascular accident. The physiatrist, neurologist, internist, physiologist, and many others should pursue the problem. We issue the challenge.

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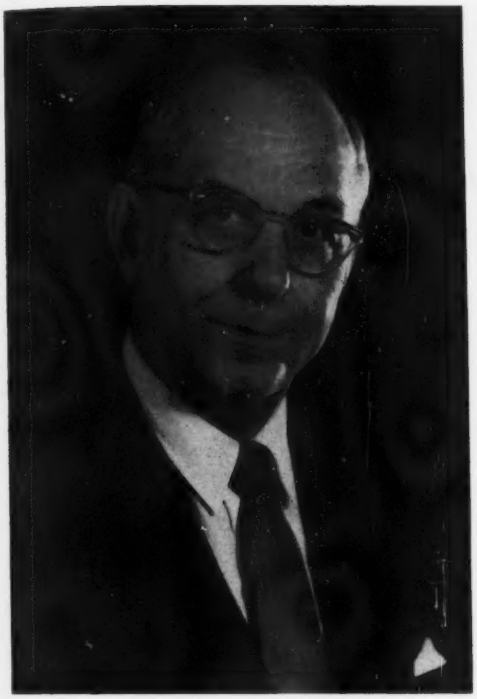
Discussion (Abstract)

Dr. Claude W. Garrett, Jr., New Orleans, La. Doctor Buchanan has presented an impressive series of cases to support the value of early and vigorous treatment of the patient with a cerebrovascular accident. Without precipitating further episodes or producing extension of the disease process she has eliminated the most serious and discouraging complications seen in these patients. She has issued a challenge for more research, though her series challenges all physicians to achieve the same excellent results in therapy.

Higher Standards of Excellence



MILFORD O. ROUSE, M.D.

Throughout the years the Southern Medical Association has achieved an enviable reputation of high quality in its scientific programs —general sessions, section papers, exhibits and Journal. The even greater excellence of the scientific program which awaits registrants at the Atlanta Session, November 16-19, will reflect not only hours of faithful, productive work by Section Officers and others, but also the fruitful work of the new Committee on Scientific Work, serving as a catalyst, as it were.

The Sections of Southern have always had a large degree of autonomy, and always should. It has been a tribute to the ability and diligence of Section Officers that program quality has been maintained often without any special coordination or continuity. But with the increasing competition among many excellent medical organizations for the time of the busy modern practitioner, especially the younger physician, the Council realized that nothing should be taken for granted, but that every means should be utilized to keep Southern doctors preferring Southern Medical.

Therefore, a special Committee on Scientific Work was appointed, consisting of Dr. A. Clayton McCarty as Chairman, ably assisted by Dr. Julian Ruffin, Dr. J. Morris Reese, Dr. Lenox D. Baker, and Dr. May Owen. A very successful "get-together" was held in New Orleans last November, and then for the first time in Birmingham in February the new Committee brought together the Secretaries or Chairmen of the twenty Scientific Sections. After an evening and full day of exchange of problems and ideas, there emerged the framework of what appears to be the best program in years, ready for the Atlanta session. Of particular value was the planning of several joint programs.

The Committee on Scientific Work has also pointed out the very practical value of an Executive Committee selected by each Section. Such a group advises on possible program material and evaluates such when presented in addition to giving careful thought to the nominations of Section Officers. Most Sections now have such Executive Committees.

There have been planned two symposia of unusual interest and merit—on Nuclear Medicine, and on the Problems of Senior Citizens, or Geriatrics. On the opening Monday in Atlanta will be excellent general sessions in Medicine and in Surgery. At the Tuesday noon luncheon will be a special message from the AMA President from the South, Dr. Louis Orr of Orlando, Florida.

Section Officers have also shown much interest in securing timely and informative scientific exhibits. The Technical Exhibits, always excellent, give promise of being even better.

Atlanta, the Queen of the Old South, is well known for its cordial hospitality, and Atlanta and Georgia doctors and their wives are making plans to assure that every Southern visitor the week of November 16 will go home feeling that he and she have had the most pleasant time of a lifetime.

And behind the scenes—but in the middle of all the activities, the members of our faithful Headquarters Staff are functioning superbly.

Your President is most grateful for the enthusiastic, fruitful work on the part of hundreds, and he cordially invites every physician and his wife in the South to enjoy with him and his wife the best Southern meeting in years.

MILFORD O. ROUSE, M.D.
President

President's Page of the Woman's Auxiliary

This has been a good year for the Woman's Auxiliary with everything running smoothly and each Officer, Chairman and Councilor cooperating in every way. There has been a close association between members of the Board which has been very gratifying and which has expedited the work of the President.

CONVENTION—Now that November is nearly here, everyone is making plans to attend the Convention in Atlanta. Those who were fortunate enough to have attended the previous meeting of the Southern Medical Association there will remember the friendliness and hospitality of that city. The headquarters for the Woman's Auxiliary will be the Henry Grady Hotel. Mrs. Henry Steadman and her committees have planned three days of most delightful entertainment. Besides all the social affairs planned for both the doctors and their wives jointly, the women will have time for shopping and a Fashion Show and Tea at Rich's Department Store, an historical bus tour of Atlanta and a tour of homes followed by tea at the Art Museum.

Besides the Pre-Convention Board breakfast on Monday and the Post-Convention Board breakfast on Wednesday, the only session of business will be on Tuesday morning. The annual Doctor's Day Awards luncheon, which is always the highlight of the Auxiliary meeting and to which the women invite their husbands, will be held this year on Wednesday.

NEWS ITEMS—We have heard many news items of interest to the Southern Auxiliary. Mrs. Harvey Garrison has found it necessary to resign as Parliamentarian and Mrs. Shelley Davis will serve in her place. We have received many sad notices of the passing of loved ones: Mary Curtis' father and the husbands of three of our Past-Presidents, Dr. J. N. Brawner; Dr. V. E. Holcombe; and Dr. O.

Mrs. George W. Owen

Continued on page 1157

EDITORIALS

CAUTION IN ACCEPTANCE OF THE NEW

Much has been written on "Modern Concepts of Medicine" but still a physician must constantly study and compare old modalities with the new modalities. In the various specialties we have seen the pendulum swinging back and forth.

The horrors of the x-ray and radium have been portrayed recently by both physicians and the press, and yet there is no true foundation for this accusation of a fine modality. Of course, they have been talking about general body irradiation, but they have made the public fear even having an x-ray film made. Could it be possible that more mutations in the testes might be caused from the wearing of tight pants than from having many x-ray pictures made? Most physicians have an x-ray machine for making pictures, or give orders for a roentgenogram several times a day; therefore, they can make positive efforts and take means to help lower the radiation dosage to the gonads to the lowest level consistent with the best standards of medical practice. Scott Wendell[1] suggests that in the first 30 years of life the gonadal dose should be strictly limited according to published recommendations. In later years of life, beyond the reproductive period, the genetic (gonadal) effects are of no clinical significance. He recommends the following:

1. Take only pictures that are absolutely essential.

2. Discourage health insurance policies that include free x-ray examinations.

3. Limit fluoroscopic examinations to specific purposes, especially in children. *Keep in mind* that one minute of continuous fluoroscopy can be equivalent in radiation to 400 chest films.

4. Teach x-ray technicians the importance of lowering the gonadal dose with adequate testicular and ovarian shields.

5. Reduce the quantity and improve the quality of the x-ray beam by using filtration and greater distance.

6. When possible delay abdominal and pelvic exposure on pregnant women until the last trimester.

At a recent medical meeting it was interesting to hear a physician discuss a paper on acne, who four years previously had thrown away the valuable tool of irradiation of the skin for acne in favor of antibiotics and steroids. Now the pendulum has swung back and he finds that these young people may have been damaged more by, (1) the use of steroids as to sperm counts and enlargement of breasts in the male, and with (2) damage to the immune mechanism against bacteria from prolonged use of antibiotics, than ever was produced by conservative irradiation of the skin. The gonads can be successfully protected by lead shielding in all routine x-ray treatment of the skin. This latter modality provides permanent cures in many cases, while the former may be successful only while the patient is under treatment.

The drug companies have urged us all to use the cortisones and their various derivatives in all skin diseases. But the endocrinologists have told us from the first that there are many other steroids from the adrenal glands and that the use of one potent steroid may be dangerous. This has been proven as the steroids have been used unsuccessfully for everything from lichen planus to psoriasis. It has been known by the conservative dermatologist from the beginning that cortisone is beneficial in only a few diseases and that it is contraindicated in others. Seemingly, however, a steroid has to be tried by everyone on every skin disease before these patients are referred to the dermatologists.

Dermatologists are now receiving many patients whom they used to cure and who now seem to be resistant to all treatment because they had been placed on steroid therapy by other doctors and even by other dermatologists. It is a fact that the cortisone group of substances is indicated for only four skin diseases: (1) acute pemphigus, (2) acute lupus erythematosus, (3) acute drug eruptions, (4) acute urticaria.

In the first two diseases the drug is used continuously and must be used for a long

1. Wendell, Scott: The Clinical Radiologist and the Problems of Radiation Hazards, J.A.M.A. 170:421, 1959.

time. In these conditions it is suspected that the lapse of even a few weeks in steroid administration may produce antihormones and the drug is then of no value or huge doses become necessary.

In the second two diseases it is known that these should be given in large doses at first, gradually tapering off within two weeks. If they do not improve, other old-fashioned methods of treatment must be tried; these were curative in many cases before the advent of cortisone.

The psoralens and the antimalarials quinacrine (Atabrine), chloroquine (Aralen), and hydroxychloroquine (Plaquenil) are excellent new drugs. The latter are used in the treatment of lupus erythematosus, light sensitive eruptions, recurrent multiple skin cancers from the sun (also perhaps xeroderma pigmentosa, with loss of pigment with the beginning of skin cancers in early life) and the psoralens are effective in vitiligo. The latter seems to thicken the skin and cause more pigmentation. It is a furocoumarin and has a photodynamic action in the skin with the addition of sunlight. It is being used in such diseases as vitiligo and farmer's and sailor's skin with multiple skin cancers. The antimalarials seem to screen out ultraviolet light in the range from 3100°-3300A units. However, some patients taking the drug seem to become clear of their eruption but still have sunburn. The minimal erythema dose seems to be reduced with both drugs.

Let us not, however, be too quick in accepting these drugs universally and give them to all thin-skinned, "Irish-type" individuals so they can get out in the hot sun and enjoy the exhilaration of sun bathing and that deep, dark tan. I still believe these people should enjoy the early morning and late evening sun; that they should use sun screens in ointment and liquid form, if they have to be out for short periods in the middle of the day; and that they should protect their skin as their forefathers did with clothing, hats and gloves. These people, even with protection, are candidates for skin cancer in later years. When they take a new drug to make them less sensitive to sunlight I believe they will overdo a good thing and may be upsetting Nature's balance to the various rays of the sun. Later they may become sensitive to the one ray of light from which the drug has not protected them. Several of our cases of light sensitivity, we believe, have become sensitive to blue light by screening out the ultraviolet light with drugs or tinted window glass in cars.

The wife of a doctor wished to go to Hawaii without sunburning. She was of the fair-skinned Irish type. She was placed on 250 mg. of chloroquine twice daily, and came back from Hawaii nicely freckled and she had not been sunburned. This drug was given up during the winter and the following April, while working outdoors, she developed a light sensitive polymorphic eruption of the plaque-like type which was cleared only after 4 months of intensive testosterone therapy. Thus, it is the belief that while preventing her from sunburning she also developed an allergy to one ray of light, possibly the shorter ultraviolet rays or the rays above 3300A from which she was not screened.

In conclusion, we wish to stress to all general practitioners and specialists that we use the old modalities of treatment and only slowly recommend new treatment except in research and experimental programs.

JOHN H. LAMB, M.D.

"MICTURITION SYNCOPE"

Early in a brief career in general practice your Editor was called out one night to see a healthy young man who, while urinating following awakening from a sound sleep, toppled over in a faint and struck his head on the bath tub. Two or three stitches were needed for the scalp laceration.

Over the years several patients have either voluntarily or upon direct questioning offered the story, usually of awakening from a sound sleep, taking a few short steps to the bathroom and upon beginning to urinate, having an uncomfortably distended bladder, have fainted. In fact, the story has been amplified upon occasion that after such episodes, or near episodes the man has preferred to void in the sitting position if he has just awakened, recognizing the interrelationship of having slept to assuming the erect position in urination. Only rarely may such a person have a slight sense of faintness at the beginning of micturition when he has been active in the daytime. Furthermore, if such a patient has been awake for a time before arising to void the faintness is not noticed.

In the subsequent more than three decades

of teaching medical students, your Editor has alluded to this type of syncope time and time again, at the bedside or in the clinic, in differential diagnosis, and at times has developed the history in the student's presence.

Never having thought of this as being particularly unusual, and having assumed an acceptable physiologic basis for this occurrence in a man, the topic was never looked for in the literature or discussed with confreres. Thus, your Editor was amazed to read only recently a report of seven such instances with a statement that this type of syncope had never been described in the literature.[1] On the heels of this report came the description of two cases as published in this issue.[2] This physiologic disturbance which may occur in healthy men is worthy of comment, since it probably is not uncommon if searched for, and because of the almost unbelievable fact that it has had no attention in the literature.

Both Proudfit and Forteza, and McGee have called attention to the onset of this syncope in healthy men of younger years, with episodes occurring commonly at widely spaced intervals. (Dermksian and Lamb[3] in a general consideration of syncope in young men in Air Force personnel mention four instances of syncope at urination in a total of 82 subjects having had syncope.)

Your Editor, having had his attention called to this type of syncope early in his career by a fortuitous circumstance, has loosely rationalized as follows, to account for the decreased cerebral blood flow. A person in sound slumber has some degree of hypotension, he awakens, and quickly gets up, takes a few steps to the bathroom and stands motionless. Postural hypotension added to the hypotension of sleep seemed to be part of the answer, since the histories indicated that if wakefulness had been present before arising, faintness did not occur. An additional factor seemed the quick emptying of a distended bladder, dropping intra-abdominal pressure with pooling of blood in the splanchnic area, akin, possibly, to the syncope in the operating room nurse or intern assistant who may stand motionless, or the soldier standing at attention.

Proudfit and Forteza[1] bring the Valsalva maneuver into the physiologic picture. They quote from authors interested in cough syncope and who had studied the effects of this maneuver upon the circulation in normal persons. It has been found that straining raises the intracranial, intrathoracic, and intra-abdominal pressures, that central venous pressures are increased, and that the "net pressure" in the arteries in these body cavities may fall. These factors lead to a "displacement of blood from vessels in the body cavities to regions of the body that are not subjected to increased extravascular pressure, such as the skin, muscles, scalp and extremities."[1] As a result the output from the left ventricle is decreased. Derbes and Kerr[4] in combining the factors in cough syncope point to McCann's findings of a marked rise in right ventricular pressure during cough in two patients having the syndrome. With the Weber experiment (Derbes and Kerr point to the fact that Weber, in 1851, described in detail the physiologic results of the maneuver attributed to Valsalva who merely advanced it for ear disease) the blood pressure in one patient dropped to 50 mm. in the interval of one beat. In the analysis of physiologic factors in micturition Best and Taylor[5] state, "Though the abdominal muscles play a non-essential part in micturition, the act, under ordinary circumstances, is started by the contraction of these muscles; . . . the flow of urine is also accelerated during micturition by the rise in intra-abdominal pressure induced by the voluntary contraction of the abdominal muscles." Here is the basis for the Valsalva (or Weber) maneuver at the beginning of urination. With better developed abdominal musculature one would expect this physiologic syncope to occur in young men rather than in older ones or in women.

Proudfit and Forteza indicate that the circulatory phenomena of the Valsalva maneuver do not completely explain micturition syncope pointing out that it occurs with micturition "only after prolonged recumbency." To which your Editor would like to add and re-emphasize that his occasional patients have recognized that faintness does not occur if

1. Proudfit, W. L., and Forteza, Mario Enrique: Micturition Syncope, New England J. Med. 260:328, 1959.
2. McGee, Robert R.: Micturition Syncope. Report of Two Cases, South. M. J. 52:1076, 1959.
3. Dermksian, George, and Lamb, L. E.: Syncope in a Population of Healthy Young Adults, J.A.M.A. 168:1200, 1958.
4. Derbes, Vincent J., and Kerr, Andrew: Cough Syncope. Springfield, Ill., Charles C. Thomas, Publisher, 1955, p. 114.
5. Best, Charles H., and Taylor, Norman B.: The Physiological Basis of Medical Practice. Baltimore, Williams & Wilkins Co., 1955, p. 483.

there has been a period of wakefulness before emptying even an uncomfortably distended bladder, and that on occasion a patient prophylactically uses the female position in voiding if he has just awakened, recognizing the syncope or faintness as related to micturition *only* if he has just awakened.

One wonders if certain physiologic aspects of sleep,—a level of systolic pressure below the waking normal, slower pulse rate, lessened tone of peripheral blood vessels, and the minimal tone of skeletal muscle, are not indicative of a decreased peripheral resistance which, on sudden awakening and assuming the erect posture, permit even a greater degree of temporary postural hypotension than in waking hours.[6] All of these items would be enhanced by the Valsalva effect of beginning micturition. This thinking would explain the micturition syncope only following slumber and its avoidance by urination in the sitting position.

It is surprising that a physiologic phenomenon should have attracted so little attention in the literature, and one can only wonder how common this is when inquiry is made.

6. Kampmeier, R. H.: Physical Examination in Health and Disease. Philadelphia, F. A. Davis Co., 2nd Ed., 1957, p. 500.

25 YEARS AGO

Functional Disability in the Pulmonary Fibroses*

"Pneumonoconiosis presents a medicolegal problem of major importance. Many studies exist which deal with its etiology and pathogenesis and its diagnosis by roentgenograms, but so far little attention has been paid to its physiologic aspects, though their practical importance is obvious. Especially is this so in view of the growing tendency to adjust awards of workmen's compensation to the degree of disability. In order to do this properly it is essential that objective means of estimating disability be sought which will be fair alike to workman and employer. With this in mind we have carried out investigations on the respiratory function of fifty-three cases of pulmonary fibrosis of various types, not all of which were pneumonoconioses.

". . . We will confine ourselves at this time to a discussion (1) of the correlation of roentgenographic studies with the measurements of the pulmonary capacity and of the saturation of the arterial blood with oxygen, and (2) of our observations on the ventilation of the lung during exercise.

"The total pulmonary capacity and its subdivisions were measured by the method of Christie. . . .

"In order to determine to what extent the roentgenograms of the lungs give clues as to the degree of functional impairment of respiration, the fifty-three cases of pulmonary fibrosis were divided into six groups, according to the anatomic type of fibrosis revealed. . . .

Conclusions

"1. The comparison of the observed with the normal calculated pulmonary capacity in cases of pulmonary fibrosis indicates that a decrease in the total and vital capacities and an increase in the residual air are characteristic changes in this condition. These changes tend to become more accentuated as the degree of fibrosis increases, but frequent exceptions to this correlation emphasize the fact that one cannot judge accurately the degree of abnormality in pulmonary capacity from roentgenograms alone.

"2. The ratio of residual air to total pulmonary capacity is one of great functional significance; the higher the ratio the greater is the tendency to anoxemia. Thus the saturation of the arterial blood with oxygen is less than the normal 94 per cent in every case in which the ratio exceeded 49 per cent, in all but one case in which it exceeded 45 per cent, and in all but four cases in which it exceeded 40 per cent.

"3. The Sturgis-Peabody formula for predicting maximal ventilatory capacity from the vital capacity is shown to be roughly correct when applied to cases of pulmonary fibrosis. In a group of twenty-five patients with pulmonary fibrosis, comparison of the percentage of normal vital capacity observed with the percentage of normal maximal ventilatory capacity predicted by the formula gave a correlation coefficient of 0.526 ± 0.1349, indicating that further work is needed in order to devise a better formula.

"4. Patients with pulmonary fibrosis attain maximal ventilation with less acceleration in rate of breathing than in the case of normal subjects or patients with heart disease or emphysema. We are continuing our observations in the belief that a higher correlation between vital and ventilatory capacity will be attained if the effective alveolar ventilation is measured."

*McCann, W. S., Hurtado, Alberto, Kaltreider, Nolan, and Fray, Walter W.: The Estimation of Functional Disability in the Pulmonary Fibroses, J.A.M.A. 103:810, 1934.

SOUTHERN MEDICAL NEWS

ALABAMA

The following Alabama doctors will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19: Drs. William L. Poole, Birmingham, Section on Dermatology and Syphilology; Marvin Woodall, Birmingham, Section on General Practice; W. N. Jones, Birmingham, Section on Gynecology; William G. Thuss, Sr., Birmingham, Section on Industrial Medicine; Joseph Derivaux, Birmingham, Section on Ophthalmology and Otolaryngology; F. F. Schwartz, Birmingham, Section on Orthopedic and Traumatic Surgery; Joseph M. Donald and Thomas W. Mears, Birmingham, Section on Surgery.

Dr. Robert C. Berson, Dean of the Medical College and Vice-President for Health Affairs of the University of Alabama, announces the appointment of Dr. Robert Earl Roth as Chairman of the Department of Radiology at the University of Alabama Medical Center.

Dr. Walter B. Frommeyer, Jr., has been installed as President of the Alabama Heart Association. Dr. Frommeyer is Professor and Chairman of the Department of Medicine at the University of Alabama Medical Center.

The Jefferson County Medical Society presented its Distinguished Services Award to Dr. Cecil D. Gaines for his leadership as Chairman of the Grievance and Medical Ethics Committee.

ARKANSAS

At the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19, the following Arkansas doctors will present papers: Drs. W. T. Knicker, Little Rock, Section on Pediatrics; Fount Richardson, Fayetteville, and H. King Wade, Jr., Hot Springs, Section on Urology.

Continued on page 1163

WOMAN'S AUXILIARY

Continued from page 1152

M. Marchman. We were delighted to hear that our President-Elect and Dr. Chenault have a fine baby girl, Catherine Leigh, who was born in June.

AUXILIARY ACCOMPLISHMENTS—In accordance with the action taken at the meeting last year, the Executive Committee voted unanimously to give $1,000 remaining in the Jane Todd Crawford Fund to the Home Building Finance Committee of the Southern Medical Association. This was presented on Doctor's Day, March 30, in appreciation of our fine doctors in the Southern Medical Association.

One of the most important accomplishments this year has been the moving of the records, histories, biographies, papers and books collected throughout the years by the Auxiliary, to the SMA building in Birmingham. The Auxiliary Room Committee with the President and President-Elect have spent several days on two occasions, sorting this material so that it is in good order, filed and easily accessible to any visitors to the Auxiliary Room.

TRIPS—It has been a distinct privilege to have had the opportunity to visit all but two of the sixteen State meetings and the SMA Auxiliary in Washington, this year. When conflicts prevented a visit to the conventions in Maryland and Louisiana, Mrs. K. W. Howard, First Vice-President and Mrs. Roy A. Douglass, Second Vice-President were sent to represent the President. It is very gratifying to know in what great esteem the Southern Medical Association is held and how many loyal members and friends there are throughout our Southland. We will never forget the many courtesies extended to us nor the wonderful new friends we have made.

In conclusion, your President regrets that her year is drawing to a close. There has been much correspondence and much travel, but rewards which can never be measured. I thank the auxiliary members for making it possible for me to have had these experiences. Without the cooperation of each member of my Executive Board, Dr. Rouse, the Advisory Council, Mr. Foster and his staff with their help, encouragement and valuable assistance, all this would not have been possible. I thank each of you and wish continued success to those who will follow me in being a part, for a year, of our great Southern Medical Association.

MRS. GEORGE W. OWEN, *President,*
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BOOKS RECEIVED

"Allergic" Encephalomyelitis. Edited by Marian W. Kies, Ph.D., Chief, Section on Biochemistry, National Institute of Mental Health, Bethesda; and Ellsworth C. Alvord, Jr., M.D., Associate Professor of Neurology and Pathology, Baylor University College of Medicine, Houston, Tex. 557 pages. Springfield, Ill.: Charles C. Thomas, Publisher. Price $13.50.

Physiology of Cardiac Surgery. By Frank Gollan, M.D., Assistant Director of Professional Services for Research, V. A. Hospital, Nashville, Tenn. 96 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $4.50.

Pancreatitis. By Herman T. Blumenthal, M.D., Associate Professor of Pathology, St. Louis University School of Medicine, St. Louis, Mo.; and J. G. Probstein, M.D., Associate Professor of Clinical Surgery, Washington University School of Medicine, and Assistant Professor of Anatomy, School of Dentistry. 366 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $9.50.

Principles of Pathology. By Howard C. Hopps, M.D., Professor and Chairman, Department of Pathology, The University of Texas, Galveston. 295 pages. New York: Appleton-Century-Crofts, Inc., 1959.

Nutritional Diagnosis. By Grace A. Goldsmith, M.D., Professor of Medicine and Director, Nutrition-Metabolism Unit, Department of Medicine, Tulane University School of Medicine. 164 pages. Springfield, Ill.; Charles C. Thomas, Publisher, 1959. Price $5.50.

Care of the Surgical Patient. By Jacob A. Glassman, M.D., Assistant Clinical Professor of Surgery, University of Miami Medical School, and Raymond W. McNealy, M.D. 306 pages. Baltimore: The Williams & Wilkins Company, 1959. Price $6.50.

Cancer in Families. A Study of Relatives of 200 Breast Cancer Probands. By Douglas P. Murphy, M.D., Emeritus Professor of Obstetrics and Gynecology, School of Medicine, University of Pennsylvania; and Helen Abbey, Sc.D., Assistant Professor of Biostatistics, School of Hygiene and Public Health, The Johns Hopkins University. 76 pages. Cambridge, Mass.: Harvard University Press for the Commonwealth Fund, 1959. Price $2.50.

World Congress of Gastroenterology & 59th Meeting of American Gastroenterological Association. Washington, D. C., May, 1958. Two volumes, 1,347 pages. Baltimore: The Williams & Wilkins Company, 1959. Price $20.00.

An Atlas of Normal Radiographic Anatomy. Second Edition. By Isadore Meschan, M.D., Professor and Director, Department of Radiology, Bowman Gray School of Medicine. 741 pages, 1,446 illustrations. Philadelphia: W. B. Saunders Company, 1959. Price $16.00.

The Process of Aging in the Nervous System. Edited by James E. Birren, Ph.D.; Henry A. Imus, Ph.D.; and William F. Windle, Ph.D. 217 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $7.00.

Manual of Chest Clinic Practice In Tropical and Sub-tropical Countries. By A. J. Benatt, M.D. 97 pages. Baltimore: The Williams & Wilkins Co., 1959. Price $3.00.

Biosynthesis of Terpenes and Sterols. Ciba Foundation Symposium. Edited by G. E. W. Wolstenholme; and Maeve O'Connor. 303 pages. Boston: Little, Brown and Company, 1959. Price $8.75.

Glaucoma. Transactions of the Third Conference, January 1958. Edited by Frank W. Newell, M.D., Department of Surgery (Ophthalmology), The University of Chicago. 260 pages. New York: Josiah Macy, Jr., Foundation, 1959. Price $5.25.

The Child With A Handicap. Edited by Edgar E. Martmer, M.D., Associate Clinical Professor of Pediatrics, Wayne State University College of Medicine. 396 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $11.00.

The Brain and Its Functions. A Symposium sponsored by the Wellcome Historical Medical Library, National Hospital, Queen Square and the Institute of Psychiatry, University of London. 260 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $5.50.

Intra Vascular Catheterization. Compiled and Edited by Henry A. Zimmerman, M.D., Chief of the Cardiovascular Section Division of Medicine, St. Vincent Charity Hospital, Cleveland. 768 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $16.75.

Gynecologic Endocrinology. By Gardner M. Riley, Ph.D., Associate Professor of Obstetrics & Gynecology, University of Michigan Medical School. 313 pages. New York: Paul B. Hoeber, Inc., 1959. Price $8.50.

Tuberculosis and Other Communicable Diseases. By J. Arthur Myers, M.D., Professor of Internal Medicine and Public Health,

University of Minnesota. 427 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $14.50.

Treatment of Cancer and Allied Disease. Volume 3, Tumors of the Head and Neck. Second edition. By 70 authors, Edited by George T. Pack, M.D.; and Irving M. Ariel, M.D. 767 pages, with 1,028 illustrations. New York: Paul B. Hoeber, Inc., 1959. Price $30.00.

Navy Surgeon. By Herbert Lamont Pugh, Rear Admiral (Ret.), U.S.N. 459 pages. Philadelphia: J. B. Lippincott Company, 1959. Price $5.00.

Peripheral Vascular Diseases. By Travis Winsor, M.D., Assistant Clinical Professor of Medicine, University of Southern California School of Medicine. 817 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $16.50.

Community Mental Health. By Margaret C. L. Gildea, M.D., Assistant Clinical Professor of Neuropsychiatry, Washington University School of Medicine. 161 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $5.00.

Trigeminal Neuralgia Its History and Treatment. By Byron Stookey, M.D., Professor Emeritus of Clinical Neurological Surgery; and Joseph Ransohoff, M.D., Assistant Professor of Clinical Neurological Surgery, both of the College of Physicians and Surgeons, Columbia University. 359 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $10.75.

Therapeutic Electricity and Ultraviolet Radiation. Fourth volume of Physical Medicine Library. Edited by Sidney Licht, M.D. 343 pages. New Haven, Conn.: Elizabeth Licht, Publisher, 1959. Price $10.00.

Parasitology. (Protozoology and Helminthology). By K. D. Chatterjee, M.D., Associate Professor of Medicine, R. G. Kar Medical College and Physician to College Hospitals, Belgachia, Calcutta. Second edition, 186 pages, 94 illustrations. Calcutta: S. Bhattacharya & Co., 1959.

Your Mind Can Make You Sick or Well. By Curt S. Wachtel. 238 pages. Englewood Cliffs, N. J.: Prentice-Hall, Inc., 1959. Price $4.95.

Medical Education. Annotated Bibliography, 1946-55. World Health Organization. 391 pages. New York: Columbia University Press, 1959. Price $6.75.

Annual Review of Medicine. Volume 10. Edited by David A. Rytand and William P. Creger, both of Stanford University School of Medicine. 429 pages. Palo Alto, Calif.: Annual Reviews, Inc., 1959. Price $7.00.

V. A. Prospectus Research in Aging. From a Veterans Administration Advisory Committee on Problems of the Aging, 1958. 125 pages. Washington, D. C.: U. S. Government Printing Office. Price $1.50.

Progressive Exercise Therapy in Rehabilitation and Physical Education. By John H. C. Colson, F.C.S.P., M.S.R.G., M.A.O.T., Wakefield, England. 184 pages. Baltimore: The Williams & Wilkins Co., 1958. Price $4.50.

A Handbook of Obstetrics and Gynaecology for Nurses. By Douglas G. Wilson Clyne, B.M., B.Ch., M.A. (Oxon.), L.R.C.P., F.R.C.S. (Edin.), M.R.C.O.G., Barrister-at-law, London. 196 pages. Baltimore: The Williams & Wilkins Co., 1958. Price $4.00.

Strong & Elwyn's Human Neuroanatomy. By Raymond C. Truex, Professor of Anatomy, Hahnemann Medical College. Fourth edition. 485 pages. Baltimore: The Williams and Wilkins Co., 1959. Price $10.00.

Clinical Neurophysiology. By John Marshall, M.D., F.R.C.P. (Ed.), M.R.C.P., D.P.M. (Lond.), University of London, Institute of Neurology. 291 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $8.00.

Vision Screening for Elementary Schools. The Orinda Study. By Henrik L. Blum, M.D.; Henry B. Peters, M.A., O.D.; and Jerome W. Bettman, M.D. 146 pages. Berkeley and Los Angeles: University of California Press, 1959.

International Textbook of Allergy. Edited by J. M. Jamar, M.D., Lecturer at the University of Louvain, Denmark. 623 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $17.50.

Anastomoses Between the Leptomeningeal Arteries of the Brain. By Henri M. Vander Eecken, M.D., Professor of Medical Psychology and Agrege in Neurology, University of Ghent, Belgium. 154 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $7.50.

Vocational Rehabilitation for the Physically Handicapped. By Louise M. Neuschutz. 127 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $5.75.

Patient Care and Special Procedures in X-ray Technology. By Carol H. Vennes, R.N., B.S., University of Minnesota Hospitals; and John C. Watson, R.T., Director of Courses in X-ray Technology, University of Minnesota Hospitals, Minneapolis. 195 pages. St. Louis: The C. V. Mosby Co., 1959. Price $5.75.

The Innervation of Muscle. By C. Coers, M.D., Hospital Brugmann, Brussels University; and A. L. Woolf, M.D., Midland Centre for Neurosurgery, Smethwick, England. 142 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $9.00.

501 Questions and Answers in Anatomy. By Stanley D. Miroviannis, Ph.D., Professor of Anatomy and Chairman of the Department, Still College. 332 pages. New York: Vantage Press, Inc., 1959. Price $5.00.

Bronchography. By C. Dijkstra, M.D., Medical Superintendent of "De Klokkenberg," Sanatorium and Chest Hospital, Breda, the Netherlands. 157 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $9.50.

Hypertensive Disease. By Sibley W. Hoobler, M.D., Associate Professor of Internal Medicine, University of Michigan Medical School. 329 pages. New York: Paul B. Hoeber, Inc., 1959. Price $7.50.

Genetics, Radiobiology and Radiology Proceedings, Mid-Western Conference. By Wendell G. Scott, M.D., Chairman, Committee on Radiology, National Research Council; and Titus Evans, Ph.D., Member of Committee. 142 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $5.50.

Pathologic Physiology of Oral Disease. By Richard W. Tiecke, D.D.S., Professor of Pathology, Northwestern University Dental School; Orion H. Stuteville, D.D.S., M.D., Professor and Chairman of the Department of Maxillofacial Surgery and Chairman of the Department of Oral Surgery, Northwestern University Dental School; and Joseph C. Calandra, M.D., Professor and Chairman of the Department of Pathology, Medicine and Bacteriology, Northwestern University Dental School. 468 pages. St. Louis: The C. V. Mosby Co., 1959. Price $11.50.

Conquering Your Allergy. By Boen Swinny, M.D. 208 pages. New York: Fleet Publishing Corporation, 1959. Price $5.95.

INSTRUCTIONS TO CONTRIBUTORS

Exclusive Publication: Articles offered for publication must be contributed solely to the Southern Medical Journal.

Manuscripts: Manuscripts should be original copy, typewritten, double-spaced, with wide margins. Because of lack of space, it is necessary to limit the number of bibliographic references to twenty. Footnotes and references should conform to the following style:

1. Doe, J. E.: What You Should Know about It, New England J. Med. 243:435, 1950.

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Reprints: Reprints are available at publisher's cost. An order form will accompany author's galley proof and should be returned with the galley to the Editor.

Book Reviews: Books and monographs submitted for review should be mailed to the Editor. Acknowledgment will appear in the Journal. Selection rights reserved.

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Business Address: All correspondence related to membership, subscriptions, advertising, and other business should be addressed to the Southern Medical Association, 2601 Highland Avenue, Birmingham 5, Alabama.

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53rd ANNUAL MEETING

Atlanta, Georgia

November 16, 17, 18, and 19, 1959

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CLERMONT	4.00- 5.50	6.00- 7.50	7.00- 7.50	10.00-15.00
COX CARLTON	5.50- 6.50	8.00- 9.00	8.00- 9.00	16.00-18.00
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GEORGIA	5.00 8.00	7.00-12.00	8.50-12.00	18.00-25.00
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SOUTHERN MEDICAL NEWS

Continued from page 1157

DISTRICT OF COLUMBIA

District of Columbia doctors who will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are as follow: Drs. George J. Stuart and Louis Schwartz, Section on Allergy; Raymond Allen Osbourn, Section on Dermatology and Syphilology; Irving B. Brick, Section on Gastroenterology; Milton C. Coby, Section on Orthopedic and Traumatic Surgery; Oscar B. Hunter, Jr., and C. Barrie Cook, Section on Pathology.

Major General Leonard D. Heaton has been appointed by President Eisenhower to the post of Surgeon General of the Army. The appointment was confirmed by the Senate. General Heaton has been serving as Commanding General of Walter Reed Army Medical Center.

Newly elected officers of the Clinical Club of Washington are as follow: Dr. Max J. Fisher, President; Dr. Vincent L. O'Donnell, Vice-President; and Dr. Otto T. Englehart, Secretary-Treasurer.

Dr. Robert E. Moran has been elected to honorary fellowship in the American Association of Plastic Surgeons. He is the youngest physician to receive this honor.

Dr. Edward D. Freis has been appointed Senior Medical Investigator for the Veterans Administration.

Dr. William H. Kessenich was appointed Medical Director of the Food and Drug Administration recently. He has been Acting Director since January.

Dr. S. Ross Taggart is the President-Elect of the American Venereal Disease Association. He was chosen at the 10th Annual Symposium on Recent Advances in the Study of Venereal Diseases.

Dr. Agatha J. Sobel has been appointed to the post of staff psychiatrist in the Legal Psychiatric Services Division of the Bureau of Mental Health.

Dr. Robert J. Bosworth was recently presented with the Service Award of the Year by the Sibley Memorial Hospital Alumni Association. Dr. Bosworth is Chairman of the Executive Committee and head of the medical staff of Sibley Hospital.

Dr. Eugene J. McDonald has been elected to serve as Councilor to the American College of Radiology by the District Medical Society's Section on Radiology.

Dr. Irving B. Brick has been made a Fellow in the American College of Physicians, and Dr. Jack P. Segal was made an Associate Member at the recent convocation of the College.

Dr. Charles Rath was recently appointed Secretary-Treasurer of the National Blood Club.

Promoted to the rank of Assistant Professor of Medicine at Georgetown University School of Medicine are Drs. Leonard S. Berman, Paul R. McCurdy, and Peter C. Luchsinger.

Colonel Frank M. Townsend, USAF, MC, has been appointed Director of the Armed Forces Institute of Pathology. He is the first Air Force Officer to assume the Directorship of the Institute.

FLORIDA

Florida doctors presenting papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are Drs. John T. Stage, Jacksonville, Section on Anesthesiology; H. B. Goodwin, Jr., Fort Pierce, Section on General Practice; J. Allen Offen, Miami, Section on Gynecology; Paul W. Boyles, Miami, Section on Medicine; S. B. Forbes, Tampa, Richard T. Farrior, Tampa, and Frederick E. Hasty, Coral Gables, Section on Ophthalmology and Otolaryngology; Arthur H. Weiland, Coral Gables, William S. Hatt, Sarasota, Eugene L. Jewett, Orlando, Walace E. Miller, Miami, and Lee J. Cordrey, Tampa, Section on Orthopedic and Traumatic Surgery; Richard T. Smith, Gainesville, Section on Pediatrics; and Nila K. Covalt, Orlando, Section on Physical Medicine and Rehabilitation.

The Seventh Annual Session of the Florida Diabetes Association will be held October 29, 30, at the Balmoral Hotel, Miami Beach. For further information write Dr. Morris B. Seltzer, 614 N. Peninsula Drive, Daytona Beach, Secretary-Treasurer.

GEORGIA

At the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, November 16-19, the following Georgia doctors will present papers: Drs. Mason I. Lowance, Atlanta, Section on Allergy; J. R. McLaren, Atlanta, Section on Gastroenterology; Charles W. Hock, Augusta, Section on General Practice; Sallye Toniette, Atlanta, Section on Gynecology; Miss Doris Grigg, Atlanta, Section on Industrial Medicine and Surgery; Drs. Robert H. Franch, Atlanta, and Edward R. Dorney, Atlanta, Section on Medicine; Charles E. Dowman, Atlanta, and George W. Smith, Augusta, Section on Neurology and Psychiatry; Ben H. Jenkins, Newnan, Wesley C. Thomas, Brunswick, and Truett J. Bennett, Atlanta, Section on Ophthalmology and Otolaryngology; Loui G. Bayne, Atlanta, and Jack Hughston, Columbus, Section on Orthopedic and Traumatic Surgery; Robert J. Peace, Atlanta, Section on Pathology; Joseph Yampolsky, Atlanta, Section on Pediatrics; Arthur M. Pruce, Atlanta, Section on Physical Medicine and Rehabilitation; Bryan L. Redd, Jr., Atlanta, Robert B. Quattlebaum, Atlanta, Ted F. Leigh, Atlanta, and John R. McLaren, Atlanta, Section on Radiology; J. P. Woodall, Macon, and Garland D. Perdue, Atlanta, Section on Surgery; William H. Bennett, Atlanta, and Harold P. McDonald, Atlanta, Section on Urology.

Dr. Charles T. Brown, Guyton, has been named Medical Director of the Bullock County Department of Public Health.

Dr. Abram Goldsmith, Albany, has been named Diplomate of the American Board of Obstetrics and Gynecology.

Dr. Leonard T. Maholick, Columbus, has been installed as President of the Georgia Psychiatric Association.

Dr. Richard W. Blumberg, Atlanta, will become Chairman of the Department of Pediatrics at the Emory University School of Medicine.

Dr. Joseph H. Patterson, Atlanta, is the Chief Physician of the new Henrietta Egleston Hospital for Children.

The new President-Elect of the Georgia Public Health Association is Dr. T. O. Vinson, District Director of Public Health for the DeKalb-Rockdale district.

KENTUCKY

The following Kentucky doctors will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19: Drs. Samuel A. Overstreet, Louisville, Section on Gastroenterology; George S. Allen and James E. Skaggs, Jr., Louisville, Section on General Practice; and Joseph B. Parker, Lexington, Section on Neurology and Psychiatry.

The Kentucky Heart Association elected Dr. Frank H. Moore, Bowling Green, President, and Dr. Marc J. Readon, Covington, First Vice-President at the 10th Anniversary Meeting of the Association.

Dr. Leslie Van Nostrand has been appointed Medical Director of the General Electric's Appliance Park, Louisville. He will succeed Dr. Alden E. Terry.

At the annual meeting of the Kentucky Society of Internal Medicine, Dr. Carl Fortune, Lexington, was chosen President-Elect and Dr. George W. Pedigo, Louisville, was installed as President of the Society for 1959-60.

Dr. Maurice Kamp, Louisville, has been elected President of the Kentucky Epidermiological Society.

Dr. Daryl P. Harvey, Glasgow, has just been appointed by President Eisenhower as a member of the President's Citizens Advisory Committee on the Fitness of American Youth.

LOUISIANA

Louisiana doctors who will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are as follow: Drs. John H. Dent and Henry D. Ogden, New Orleans, Section on Allergy; C. Barrett Kennedy and James W. Burks, New Orleans, Section on Dermatology and Syphilology; Daniel H. Winship and Charles C. Sprague, New Orleans, Section on Gastroenterology; Jason H. Collins, New Orleans, Section on Gynecology; J. William Crookshank, Lake Charles, Dabney M. Ewin, New Orleans, and Howard Karr, New Orleans, Section on Industrial Medicine and Surgery; Theodore L. Soniat, New Orleans, and Frederick H. Davis, New Orleans, Section on Neurology and Psychiatry; Jack R. Anderson, New Orleans, Jack W. Pou, Shreveport, and George G. Ellis, New Orleans, Section on Ophthalmology and Otolaryngology; G. Gernon Brown, Jr., New Orleans, Section on Orthopedic and Traumatic Surgery; Claude W. Garrett, Jr., New Orleans, Section on Physical Medicine and Rehabilitation; Isidore Cohn, Jr., New Orleans, and H. Whitney Boggs, Jr., Shreveport, Section on Proctology; Seymour Ochsner, New Orleans, Section on Radiology; Alton Ochsner, Oscar Creech, Jr., and A. N. Houston, New Orleans, Section on Surgery.

MARYLAND

The following Maryland doctors will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19: Drs. Leslie N. Gay, Baltimore, Section on Allergy; Raymond C. V. Robinson, Baltimore, Section on Dermatology and Syphilology; William D. Wheat and Charles Van Buskirk, Baltimore, Section on Neurology and Psychiatry; Robert A. Robinson, Baltimore, Section on Orthopedic and Traumatic Surgery; James R. Rooney II, Frederick, and John A. Wagner, Baltimore, Section on Pathology.

Drs. Dorothy C. Holzworth and Ian S. H. Harper have been certified as Fellows of the American Society of Anesthesiology. Drs. Margaret A. Clark, Bethesda, Harold M. Eccleston, Jr., Salisbury, and Norman B. Hollingsworth, Baltimore, have been certified as Diplomates of the Society.

The University of Maryland School of Medicine Alumni Association's honor award was presented to Dr. Edgar B. Friedenwald, Baltimore.

Dr. John Maxwell Byers, Cecil County Health Officer, has been honored for serving twenty years with the health department.

Dr. Wilbur N. Baumann, Cambridge, Dr. Irvin G. Hoyt, Queenstown, and Dr. S. Ralph Andrews, Elkton, have been named members of the Professional

Continued on page 87

BOOK REVIEWS

Poliomyelitis. Papers and Discussions Presented at the Fourth International Poliomyelitis Conference

Compiled and Edited for the International Poliomyelitis Congress. 667 pages. Philadelphia: J. B. Lippincott Company, 1958. Price $7.50.

In the proceedings of this Fourth International Conference on Poliomyelitis, there is much emphasis on virology and the general subject of vaccination. In addition to the immunologic studies regarding poliomyelitis there is an excellent section on the enteric viruses producing diseases simulating poliomyelitis. In this regard the ECHO viruses and their classification are described as are also the Coxsackie viruses.

Among the virologic studies are included the reports of observations with the electron microscope. The problems in diagnosis encountered by viral diagnostic laboratories are considered by several of the foremost

authorities in this field. In this section of the proceedings the isolation of the virus, viruses and neutralization tests, precipitin tests and complement-fixation tests are considered. Clinical discussion relates to the derangement of respiratory physiology, the pulmonary, gastrointestinal, genitourinary and circulatory complications of the disease, and the neuromuscular factors relating to rehabilitation. The physical medicine, orthopedic, home care and vocational aspects of poliomyelitis are taken up in the concluding sections of the book.

This comprehensive volume is highly recommended and deserves a place in every medical library.

Practical Use of the Office Laboratory and X-ray, Including the Electrocardiograph

By Paul Williamson, M.D. 317 pages. St. Louis: The C. V. Mosby Company, 1957. Price $10.75.

This simply written monograph contains much information which should be useful to the general medical practitioner. The procedures are simply described and would appear to be of most benefit in the *routine* of everyday office practice. Of particular usefulness are the sections on interpretation of the laboratory results and the pitfalls involved during such interpretation. Approximately one-third of the text is devoted to "Office X-ray." Although many good points in radiologic interpretation are made, the general medical practitioner is usually (and rightfully so) unwilling to accept such full responsibility in this difficult field. The section on electrocardiography is quite brief and incomplete. No description of the now-standard V-leads is given—in fact, the author tends to belittle their importance in interpretation of the ECG. Such an omission seems hardly justified in view of recent advances in cardiology through electrocardiographic interpretation. The monograph is well illustrated, however, and should be useful to the general physician interested in designing a small office laboratory.

Neurological Basis of Behavior. CIBA Foundation Symposium

Edited by G. E. W. Wolstenholme and Cecilia M. O'Connor. 387 pages, with 109 illustrations. Boston: Little, Brown and Company, 1958. Price $9.00.

This volume is the publication of the CIBA Foundation Symposium which was held to commemorate the centennial of the birth of Sir Charles Sherrington. The papers at this symposium were presented by internationally celebrated neurophysiologists, neuroanatomists, neurosurgeons, psychologists and psychiatrists. The subjects discussed range from the early development of ideas relating the mind with the brain to the neurophysiologic basis of conditioned reflexes and behavior. Following each presentation there is a discussion and a list of references. Other subjects include the temporal lobe syndrome, the neurologic basis of responses to stress, brain enzymes and adaptive behavior, and the relevance of some neurophysiologic data to behavior disorders. The text is well illustrated by drawings, photographs, charts and graphs.

The CIBA Foundation is to be commended upon this symposium. This volume deserves a place in every library and will be of great interest to all students and practitioners who are concerned with the nervous system and its function.

Medulloblastoma

By Benjamin L. Crue, Jr., LCDR, MC, USN, Neurosurgical Service, U. S. Naval Hospital, San Diego, Calif. 181 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1958. Price $5.75.

In the preparation of this monograph, the author has had access to a large body of clinical material from several of the major neurosurgical centers in this country. After some preliminary comments regarding neoplasia in general, the pathology of medulloblastoma, including historical features and the theories regarding its pathogenesis, is described. An entire chapter is devoted to the relationship of medulloblastoma to leptomeningeal sarcoma. The remainder of this work is concerned with statistical studies regarding the incidence, age and sex distribution, symptomatology, diagnosis, treatment and prognosis. There is an excellent bibliography of about four hundred references.

This is a well written volume which includes a great deal of information about a challenging tumor. It is highly recommended to neurologists and neurosurgeons and deserves a place in all medical libraries.

Gynecologic Endocrinology

By Gardner M. Riley, Ph.D., Associate Professor of Obstetrics & Gynecology, University of Michigan Medical School. 313 pages. New York: Paul B. Hoeber, Inc., 1959. Price $8.50.

This well-written book is excellently illustrated and organized. The first section, utilizing 72 of the total 313 pages, deals with the physiology of the menstrual cycle, hormone production in pregnancy, the menstrual cycle and physiology of the breast—each chapter being related to the pituitary gland. The second and largest section is strictly clinical, up to date and very informative. The chapter on menstrual dysfunctions is especially well-written. The chapters on abnormal sexual development and the endocrine aspects of infertility are excellent. The third and last section deals with actual diagnostic procedures; various methods of hormonal analysis are given in detail. This section contains a chapter on pharmaceutical endocrine preparations, listing the various preparations and giving the structural formulae of many of them. The biologic activity of each drug is given. This reviewer could find no real faults with this book and therefore highly recommends it for general use.

1958-59 Year Book of Drug Therapy

Edited by Harry Beckman, M.D., Director, Department of Pharmacology, Marquette University Schools of Medicine and Dentistry. 534 pages. Chicago: Year Book Publishers, Inc., 1959. Price $7.50.

Little new can be added annually to the review of the Yearbook of Drug Therapy. Its function is so obvious, and anyone who has once used the book has found it so useful that one can only re-emphasize this in such an annual review. There is no other source, to the reviewer's knowledge, in which the literature of the year dealing with the use of drugs in the treat-

ment of diseases can be found. This in itself indicates the great value of the book and the repeated editions annually prove its success. One can only say that this is a book which is one of the essentials to the practicing physician.

Recent Studies in Epidemiology

Edited by J. Pemberton, M.D., Professor of Social and Preventive Medicine, The Queen's University, Belfast; and H. Willard, M.D., Co-ordinator of Rehabilitation, Cornell University Medical College. 203 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1959. Price $5.75.

Like so many recent books, this one is another collection of papers. They were presented in Holland in 1957 at the Study Group on Current Epidemiological Research, organized by the International Corresponding Club (Preventive and Social Medicine). The papers illustrative of different uses of epidemiology are in five categories: (1) The use of existing morbidity and mortality records in research, (2) field surveys or getting your own data, (3) the evaluation of health needs and services by the epidemiological method, (4) application of the epidemiological method to problems in mental health, and (5) general practice as a field for epidemiology. These papers, concerned primarily with application of the epidemiologic method, will be helpful to those contemplating similar studies.

Practical Cardiology

By Albert Salisbury Hyman, M.D., Associate Clinical Professor of Medicine, New York Medical College. 297 pages. New York: Landsberger Medical Books, Inc., 1958. Price $7.00.

This is an excellent book dealing only with the practical aspect of cardiology. It is not an encyclopedia but a good review of cardiology.

There is a definite place in modern journalism for this type of instruction and the busy physician will enjoy Dr. Hyman's forty years experience in the practice of this specialty.

The first three chapters are devoted to the history, physical examination, fluoroscopy, roentgenology, and electrocardiography. These subjects are adequately covered in an easy to read and easy to understand style. Pulmonary and cardiovascular function procedures are evaluated and properly emphasized.

The diagnosis and treatment of coronary artery disease, hypertension, and pulmonary complications of heart disease conclude this practical book which is recommended for students and general practitioners of medicine.

Electrocardiography

By Michael Bernreiter, M.D., Assistant Clinical Professor of Medicine, University of Kansas Medical School. 129 pages. Philadelphia: J. B. Lippincott Company, 1958. Price $5.00.

This is a book on the fundamental electrocardiographic findings that are seen in the every day practice of heart disease.

The basic principles of electrophysiology of the heart are adequately described and schematic diagrams clarify the more complicated electrical changes seen with bundle branch block, hypertrophy and myocardial infarction.

All usual phases of electrocardiography that are encountered by the practicing physician and students are adequately covered. The unusual and more complicated electrocardiographic phenomena are not included in this practical, easy to read manual.

Small Patients

By Alton Goldbloom, M.D., Head, Department of Pediatrics, McGill University. 316 pages. Philadelphia: J. B. Lippincott Company, 1959. Price $4.50.

This is a warm, interesting, and inspiring account of the life of one of the early leaders in the field of pediatrics. It is also the story of the early days of the establishment of pediatrics as a recognized specialty, with profiles of some of the early pioneers. This book will be enjoyable reading for anyone.

Clinical Applications of Suggestion and Hypnosis

By William T. Heron, Ph.D., Professor of Psychology, University of Minnesota. Third Edition. 159 pages. Springfield, Ill.: Charles C. Thomas, Publisher, 1957. Price $3.75.

Suggestion is universally used as a means of assuring cooperation. This short monograph discusses the effective use of suggestion and relates it to hypnosis. The author takes the point of view that the physician, dentist, or psychologist who uses hypnosis should take the role of the good teacher. That is, he gently guides the person or patient toward those objectives which the person already knows to be in his best interest.

Assuming that the professional person has already assimilated the available knowledge (theoretical and therapeutic) about suggestion and hypnosis, this monograph can serve as a practical guide to their application in the clinical situation.

Our Nuclear Adventure

By D. G. Arnott. 166 pages. New York: Philosophical Library, 1958. Price $6.00.

This succinctly composed discussion of atomic science should be a must for anyone interested in that field. Mr. Arnott has dealt with a difficult scientific subject in a manner which could make a poet a nuclear energy expert.

Initially the fundamentals are discussed including nuclear components, electrical charges and a grounding in the basic vocabulary. From here the information encompasses Japanese reports of world-wide radioactivity; the importance of atomic energy with particular reference to British needs; health and genetic hazards; and finally the political and scientific clashes are discussed.

Mr. Arnott does not believe in atomic secrets, bomb stockpiling or testing, yet he is not prepared to absolutely abolish these "neanderthal" attitudes without a realistic approach to international control of such matters.

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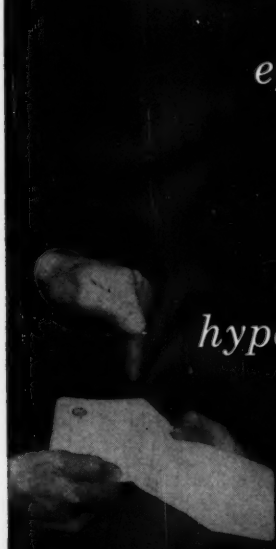


Theobarb®-R

hypotensive-sedative

EACH TABLET CONTAINS:

theobromine	*324 mg. (5 grains)*
phenobarbital	*10 mg. (1/6 grain)*
reserpine	*0.1 mg.*

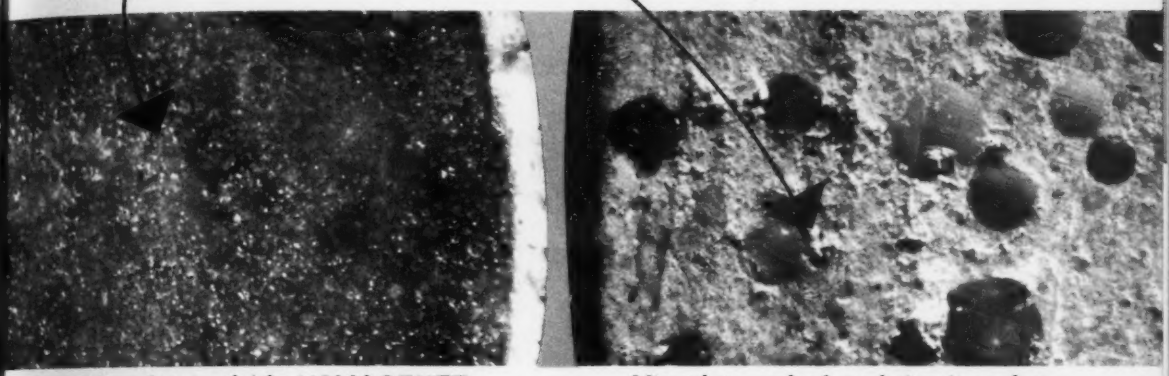
DOSAGE: One tablet 3 or 4 times daily for the first week; thereafter, not more than 2 to 2½ tablets daily.

PACKAGED IN BOTTLES OF 50 AND 500 TABLETS

Samples and literature available on request

VANPELT & BROWN, INC., Richmond, Virginia

HOMOGENIZATION makes the difference



Microphotograph of a **HOMAGENET**

Microphotograph of usual vitamin product

The photographs above point out the difference between Homagenets and many vitamin products. By means of the homogenization process, both oil and water soluble vitamins are presented in microscopic particles. Due to the fine particle size, there is much greater surface exposure, which permits quicker absorption and better utilization. This has been clinically proved by Lewis and others.[1]

1. Lewis, J.M., et al.: J. Pediatrics, *31*:496

HOMAGENETS®

The only homogenized vitamins in solid form

THE S.E. MASSENGILL COMPANY Bristol, Tennessee

Here
are the advantages
of

HOMAGENETS®*

the only
homogenized vitamins
in solid form

The advantages of HOMAGENETS

- Pleasant, candy-like flavor
- Better absorbed, better utilized
- Excess vitamin dosage unnecessary
- Longer storage in the body
- No "fishy burp"
- May be chewed, swallowed or dissolved in the mouth.

HOMAGENETS are available in five formulas:

PEDIATRIC—Children like the orange-flavored, candy-like taste.

PRENATAL—Contains iron and calcium as a dietary supplement during gestation.

GERIATRIC—A complete formula for the prevention of vitamin-mineral deficiencies.

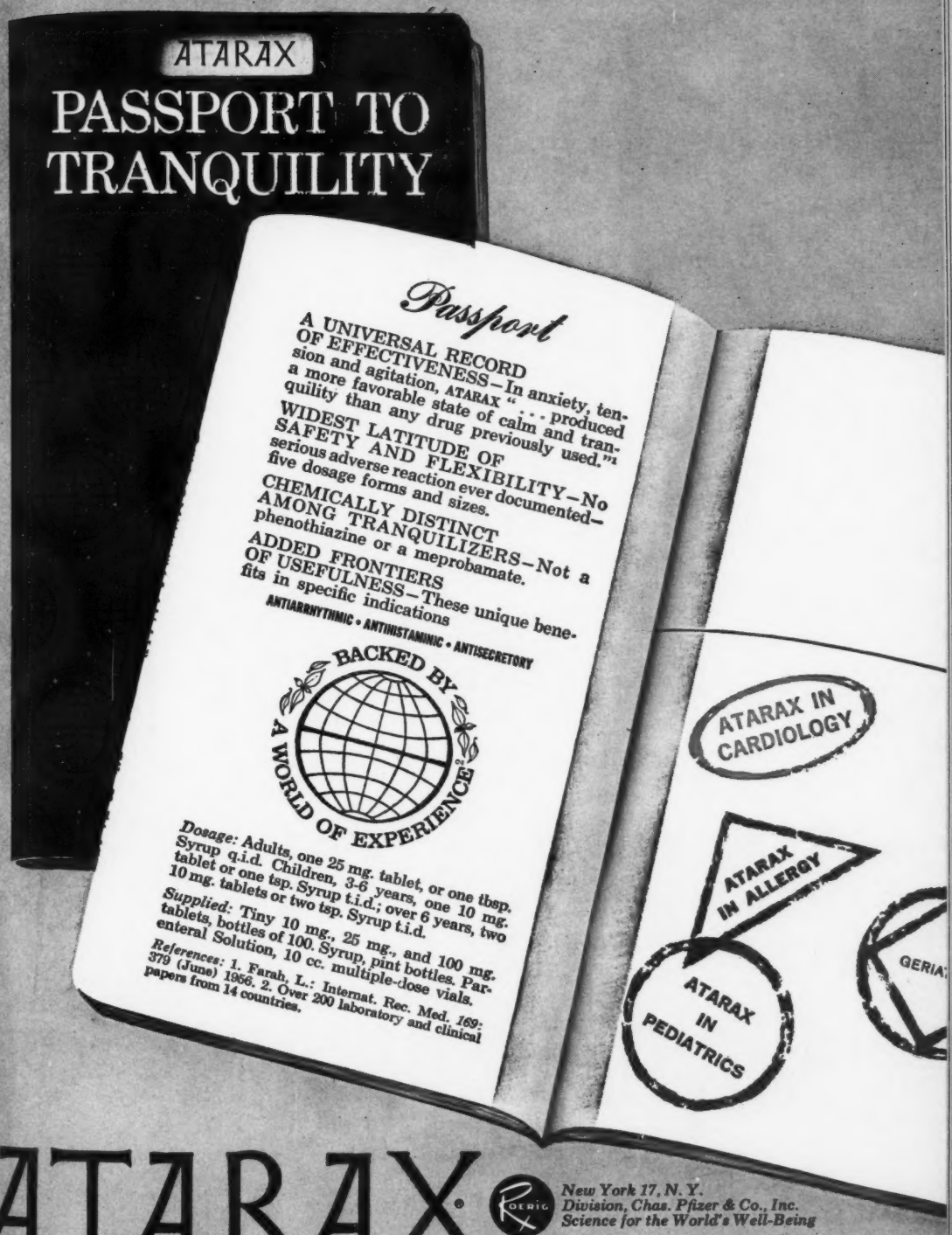
AORAL—Useful in the treatment of certain types of skin disorders.

THERAPEUTIC—Particularly indicated during convalescence and stress periods.

*U.S. Pat. 2676136. Other Pat. Pending

Currently, mailings will be forwarded only at your request. Write for samples and literature.

THE S.E. MASSENGILL COMPANY Bristol, Tennessee • New York • Kansas City • San Francisco


ATARAX
PASSPORT TO TRANQUILITY
Passport
A UNIVERSAL RECORD OF EFFECTIVENESS—In anxiety, tension and agitation, ATARAX "... produced a more favorable state of calm and tranquility than any drug previously used."1
WIDEST LATITUDE OF SAFETY AND FLEXIBILITY—No serious adverse reaction ever documented—five dosage forms and sizes.
CHEMICALLY DISTINCT AMONG TRANQUILIZERS—Not a phenothiazine or a meprobamate.
ADDED FRONTIERS OF USEFULNESS—These unique benefits in specific indications
ANTIARRHYTHMIC • ANTIHISTAMINIC • ANTISECRETORY
BACKED BY A WORLD OF EXPERIENCE
Dosage: Adults, one 25 mg. tablet, or one tbsp. Syrup q.i.d. Children, 3-6 years, one 10 mg. tablet or one tsp. Syrup t.i.d.; over 6 years, two 10 mg. tablets or two tsp. Syrup t.i.d.
Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.
References: 1. Farah, L.: Internat. Rec. Med. 169: 379 (June) 1956. 2. Over 200 laboratory and clinical papers from 14 countries.
ATARAX IN CARDIOLOGY
ATARAX IN ALLERGY
ATARAX IN PEDIATRICS
GERIA
ATARAX®
(brand of hydroxyzine)
Rx only
New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

NEW

HYDRODIURIL*

(HYDROCHLOROTHIAZ

simplifies* and improves any regimen for hypertension

*it

*it's as easy as 1, 2, 3 to use

HYDRODIURIL T.M.

(HYDROCHLOROTHIAZIDE)

Initiate therapy with HYDRODIURIL: one 25 mg. tablet or one 50 mg. tablet once or twice a day. HYDRODIURIL by itself often causes an adequate drop in blood pressure over a period of two to three weeks. This may be all the therapy some patients require.

Add or adjust other agents as required: HYDRODIURIL enhances the activity of all commonly-used antihypertensive agents; thus, the dosage of other medication (rauwolfia, reserpine, hydralazine, veratrum) should be initiated or adjusted as indicated by patient condition. If a ganglion-blocking agent is contemplated or being used, usual dosage must be reduced by 50 per cent.

Adjust dosage of all medication: the patient must be frequently observed and careful adjustment of all agents should be made to establish optimal maintenance dosage.

Supplied: 25 mg. and 50 mg scored tablets HYDRODIURIL (Hydrochlorothiazide) bottles of 100 and 1,000.
Additional literature for the physician is available on request.

HYDRODIURIL is a trademark of Merck & Co., INC. Trademarks outside the U. S. · DICHLOTRIDE, DICLOTRIDE, HYDROSALURIC.

MSD MERCK SHARP & DOHME, Division of Merck & Co., INC., Philadelphia 1, Pa.

"...iodides
and hot liquids
–[among]
the best
friends
an asthmatic
ever had."[1]

FREE YOUR ASTHMATIC PATIENT
FROM SECRETORY OBSTRUCTION
ENCOURAGE BRONCHIAL EVACUATION

ORGANIDIN®

solution and tablets — iodinated glycerol, organically bound iodine

THE WELL TOLERATED[1] IODIDE EXPECTORANT—"Wheezing" or "hacking" coughs respond most favorably to specific antitussive medication plus the "excellent bronchial evacuants"[2] —iodides—a most clinically effective type of expectorant.[3] For excellent results, add stable Organidin—organically bound iodine—to your favorite cough therapy. Organidin is better-tasting, better tolerated than inorganic iodides. Full dosage may be given immediately. **ORGANIDIN** solution is freely miscible with common syrups. **SUPPLIED:** Solution, bottles of 30 cc.; Tablets, bottles of 100. **DOSAGE:** See Physicians' Desk Reference, 1959, p. 847. (1) Seltzer, A.: M. Ann. District of Columbia **26**:17 (Jan.) 1957. (2) Segal, M. S.: J.A.M.A. **169**:1063 (Mar.) 1959. (3) McLean, J. A.: GP **18**:128 (Dec.) 1958. For professional samples and literature write:

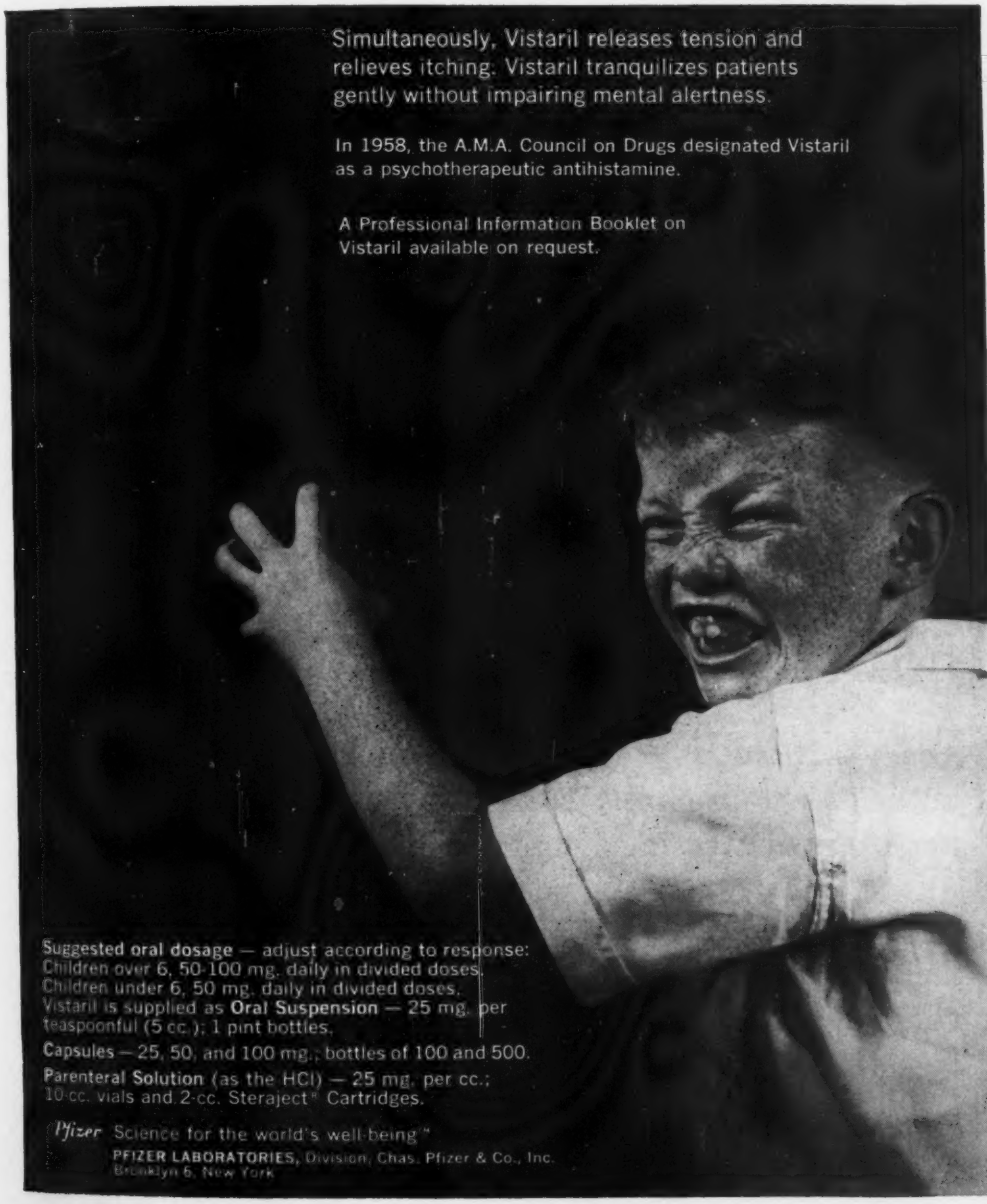
WAMPOLE LABORATORIES, STAMFORD, CONNECTICUT

VISTARIL®

hydroxyzine pamoate

ORAL SUSPENSION

restores tranquility: relieves pruritus



Simultaneously, Vistaril releases tension and relieves itching. Vistaril tranquilizes patients gently without impairing mental alertness.

In 1958, the A.M.A. Council on Drugs designated Vistaril as a psychotherapeutic antihistamine.

A Professional Information Booklet on Vistaril available on request.

Suggested oral dosage — adjust according to response: Children over 6, 50-100 mg. daily in divided doses. Children under 6, 50 mg. daily in divided doses. Vistaril is supplied as **Oral Suspension** — 25 mg. per teaspoonful (5 cc.); 1 pint bottles.

Capsules — 25, 50, and 100 mg.; bottles of 100 and 500.

Parenteral Solution (as the HCl) — 25 mg. per cc.; 10-cc. vials and 2-cc. Steraject® Cartridges.

Pfizer Science for the world's well-being®

PFIZER LABORATORIES, Division, Chas. Pfizer & Co., Inc. Brooklyn 6, New York

Al-Caroid®

controls the double trouble...

1. hyperacidity relieved – In AL-CAROID, selected antacids act promptly to relieve heartburn, flatulence and other distressing symptoms of gastric hyperacidity.

2. digestion maintained – AL-CAROID contains the proteolytic enzyme – Caroid® – which is not inactivated by antacids, thus assuring maintenance of protein digestion.

Powder/Tablets *Write for samples*

American Ferment Co., Inc. • 1450 Broadway • New York 18, N. Y.

"... which antacid? Rorer's Maalox. Excellent results, no constipation plus a pleasant taste that patients like."

MAALOX® an efficient antacid suspension of magnesium-aluminum hydroxide gel offered in bottles of 12 fluidounces.

TABLET MAALOX: 0.4 Gram (equivalent to one teaspoonful), Bottles of 100.

TABLET MAALOX No. 2: 0.8 Gram, double strength (equivalent to two teaspoonfuls), Bottles of 50 and 250.

Samples on request.

WILLIAM H. RORER, INC., Philadelphia 44, Pennsylvania

how often have you thought...

"...but how will it work in my practice?"

This most frequently asked question cannot be answered by the manufacturer, the detail man, an advertisement, a piece of mail. Only through actual experience with a product in day-to-day private practice can this question be answered.

UNITENSEN PROVED IN DAY-TO-DAY PRACTICE In office trials, Unitensen products have been proved effective therapy in the management of the hypertensive patient. These are the facts, obtained from 3,841 physicians, who used Unitensen products in their day-to-day office practice, in treating a total of 35,727 patients. In 11,093 cases (31.0%) results were "excellent"; in 51.2% (18,294) cases, "good"; "fair" results were obtained in 4,591 patients (12.9%) and in only 1,749 cases (4.9%) were results "unsatisfactory." Minor side effects were reported in 1,081 cases (3.0%).

The results mentioned above were obtained while the patients engaged in their normal daily occupations and activities. None of the patients involved in the study were hospitalized or institutionalized. And, despite such variables as dietary indiscretions, an occasional overdose, or a dose inadvertently "missed," the Proof In Practice Study shows Unitensen products to be safe, dependable, potent antihypertensive therapy . . . permitting practical office management of virtually all hypertensive cases.

UNITENSEN: BASIC HYPERTENSIVE THERAPY Although many of the patients in the Study also received diuretics and/or tranquilizers during the course of treatment, it was noted that the vasodilating effect of Unitensen was required to obtain optimum blood pressure control. Unitensen, a true hypotensive agent, is potentiated by diuretics. A combination of the two is frequently recommended for lower dosage of each drug, minimizing the side effects of either.

UNITENSEN DOES MORE THAN LOWER BLOOD PRESSURE Dr. Burton M. Cohen* makes the following observations regarding Unitensen:

"Hypotensive effect obtained through specific stimulation of afferent side of reflex pathways of blood pressure control without adrenolytic action or ganglionic blocking . . . Nausea and vomiting rare . . . No alteration of vasomotor reflexes, thus no postural collapse . . . Bradycardia, never tachycardia, may occur . . . Cardiac output not lessened . . . Renal circulation participates in reflex vasodilation . . . Cerebrovascular resistance is decreased, with improvement or maintenance of blood flow and O_2 utilization . . . No dangerous side actions have been reported."*

UNITENSEN-R® Each tablet contains cryptenamine (tannates) 1.0 mg., reserpine, 0.1 mg.

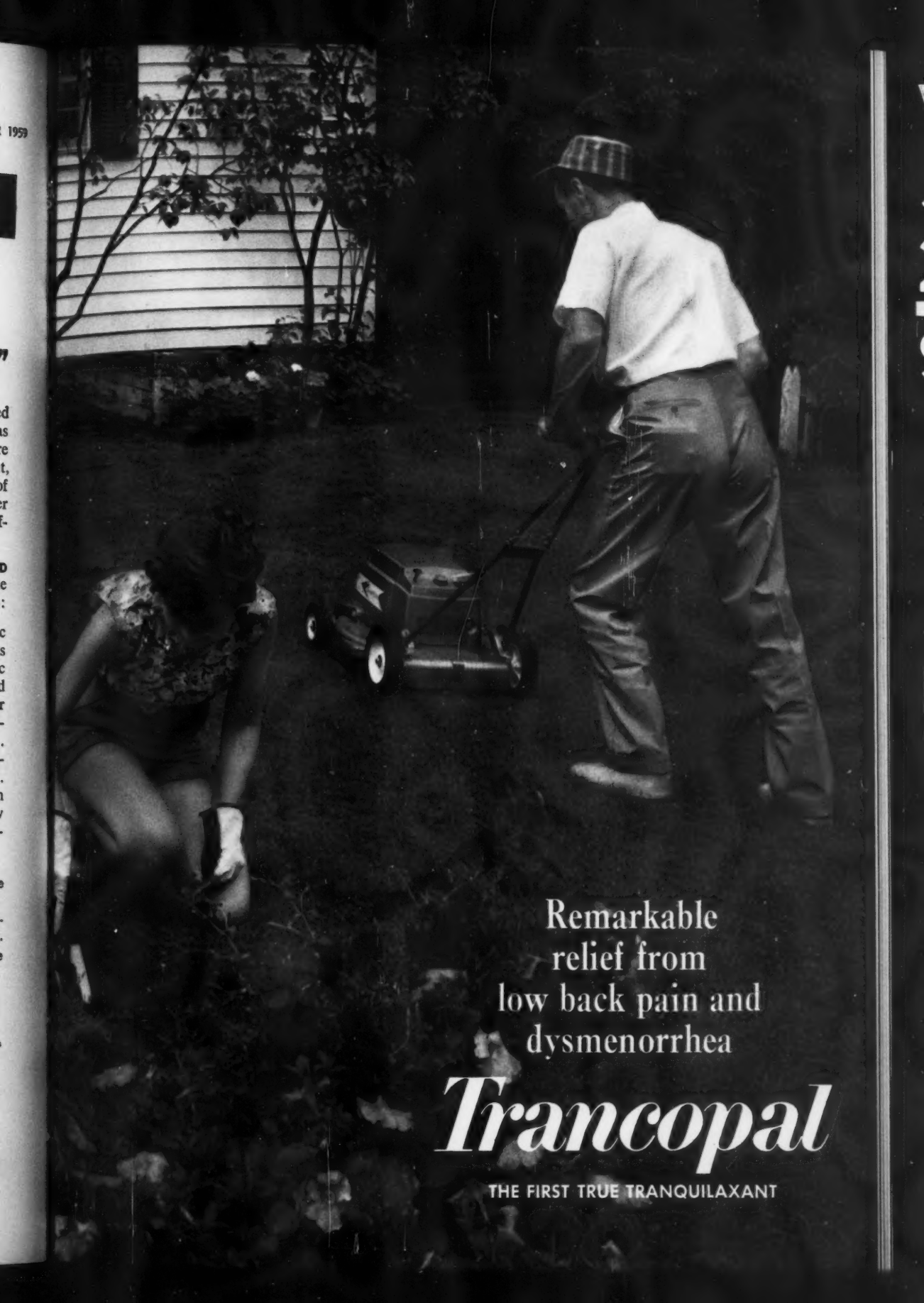
UNITENSEN-PHEN® Each tablet contains cryptenamine (tannates) 1.0 mg., phenobarbital, 15 mg.

UNITENSEN® Each tablet contains cryptenamine (tannates) 2.0 mg.

Clinical supplies available on request.

Neisler IRWIN, NEISLER & CO. • Decatur, Illinois

*Cohen, B. M.: The Ambulatory Patient with Hypertension: An Approach to Office Management, presented at the American Medical Association Convention, San Francisco, California, June 22-27, 1958.


Remarkable
relief from
low back pain and
dysmenorrhea
Trancopal
THE FIRST TRUE TRANQUILAXANT

Here wh
can expec vh
prescrib Tra

case profile no. 2758*

for low back pai for

A middle-aged man had intermittent low back pain attributed to injuries received in an automobile accident three years ago. The pain radiated down both legs, making the patient walk bent over. He also had difficulty in getting out of bed and had to pull his knees up and roll out. Any heavy lifting precipitated a new attack, and he tired easily.

Findings on x-ray of the thoracic and lumbar spine were negative. All other laboratory studies were within normal limits. A herniated disc, though still a possibility, was temporarily ruled out by the neurologic examination. Previous treatment consisted of analgesics, steroids (without success), and narcotics during severe attacks.

On a dosage of Trancopal, 100 mg. t.i.d., this patient is able to walk around almost normally and carry on his regular activities as long as he does not overdo. He has received Trancopal for over seven months with excellent relief of symptoms. There have been no side effects.

**Clinical Reports on file at the Department of Medical Research, Winthrop Laboratories.*

e what you
be when you
rib

THE FIRST TRUE TRANQUILAXANT

Trancopal®

pain for dysmenorrhea
and premenstrual tension

case profile no. 3347*

A 35-year-old housewife had a history of severe dysmenorrhea and premenstrual tension. Menarche occurred at the age of 14. She is a gravida 2, para 1. Her menstrual cycle is fairly regular, and previous medical history indicates no apparent abnormalities. Findings on pelvic examination were negative. Severe tension and irritability routinely occurred from two to seven days before and during menstruation. Cramping was experienced for all three days of the menstrual period. Analgesic preparations provided limited symptomatic relief.

Trancopal, 200 mg. t.i.d., was prescribed for dysmenorrhea. It not only has relieved the severe cramping, but has provided a welcome relief from the irritability accompanying it. Because of these excellent results, Trancopal also was prescribed for her tenseness during the premenstrual period with a most gratifying response.

This patient has successfully remained on the above regimen for over six months without adverse effects.

Turn Page for Complete Listing of Indications and Dosage

THE FIRST TRUE TRANQUILAXANT

Trancopal

potent muscle relaxant

effective tranquilizer

- In musculoskeletal disorders, effective in 91% of patients.[1]
- In anxiety and tension states, effective in 88% of patients.[1]
- Low incidence of side effects (2.3% of patients). Blood pressure, pulse rate, respiration and digestive processes unaffected by therapeutic dosage. No effects on hematopoietic system or liver and kidney function.
- No gastric irritation. Can be taken before meals.
- No clouding of consciousness, no euphoria or depression.

Indications:

Musculoskeletal:
Low back pain (lumbago, etc.)
Neck pain (torticollis, etc.)
Bursitis
Rheumatoid arthritis
Osteoarthritis
Disc syndrome
Fibrositis
Ankle sprain, tennis elbow, etc.
Myositis
Postoperative muscle spasm

Psychogenic:
Anxiety and tension states
Dysmenorrhea
Premenstrual tension
Asthma
Angina pectoris
Alcoholism

Now available in two strengths:

Trancopal Caplets®:
100 mg. (peach colored, scored), bottles of 100.

New Strength

Trancopal Caplets:
200 mg. (green colored, scored), bottles of 100.

Dosage: Adults, 100 or 200 mg. orally three or four times daily. Relief of symptoms occurs in fifteen to thirty minutes and lasts from four to six hours.

1. Collective Study, Department of Medical Research, Winthrop Laboratories.

Winthrop LABORATORIES
New York 18, New York

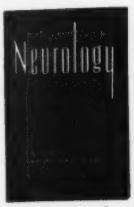
Trancopal (brand of chlormezanone) and Caplets, trademarks reg. U.S Pat. Off. Printed in U.S.A. 8-59 (1385 AM)

QUESTION:

What have authorities reported as to the efficacy of Fiorinal in tension headache?

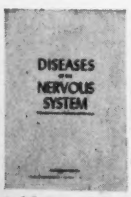
ANSWERS:

From the published reports of leading clinicians.



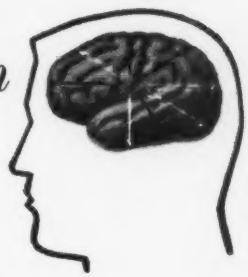
"The most effective symptomatic medication in the treatment of tension headache have been several analgesic and sedative combinations. One of the most effective is Fiorinal, which yielded relief in two out of three patients." *(Friedman, A. P., von Storch, T. J. C. and Merritt, H. H.: Neurology 4:773, Oct. 1954.)*

"In the treatment of tension headaches... [Fiorinal's non-narcotic action] offers a better opportunity for relief than some usually prescribed non-narcotic analgesics." *(Weisman, S. J.: Am. Pract. & Digest. Treat. 6:1019, July 1955.)*



"Fiorinal appears to be one of the most useful preparations to date for the relief of tension headaches. Easing of the head discomfort was accomplished by one or two tablets without any unpleasant side effects such as drowsiness or gastric upsets. In many cases Fiorinal appeared to temporarily relieve the discomfort from sinus trouble or acute respiratory infections." *(Kibbe, M. H.: Dis. Nerv. System 16:77, March 1955.)*

specific therapy for tension headache



Fiorinal®

relieves pain, muscle spasm, nervous tension

rapid action • non-narcotic • economical

FIORINAL TABLETS

Each tablet contains:
Sandoptal (Allylbarbituric acid N.F.X) 50 mg. (¾ gr.), caffeine 40 mg. (⅔ gr.), acetylsalicylic acid 200 mg. (3 gr.), acetophenetidin 130 mg. (2 gr.).

Dosage: 1 or 2 tablets every 4 hours, according to need, up to 6 per day.

SANDOZ

NEW AND EXCLUSIVE... the only 5-action, one-tablet treatment... for comprehensive control of your asthma patients, prescribe

Trademark

BRONKOTABS

THESE DISTURBING PHENOMENA — **APPROPRIATELY CONTROLLED** — **BY A ONE TABLET FORMULA:**

1. Bronchospasm	Bronchodilator	Ephedrine sulfate, 24 mg.
2. Local bronchial edema	Diuretic	Theophylline, 100 mg.
3. Allergic complications	Antihistaminic	Thenyldiamine HCl, 10 mg.
4. Tenacious mucus	Expectorant	Glyceryl guaiacolate, 100 mg.
5. Anxiety-tension	Sedative	Phenobarbital, 8 mg.

CLINICALLY PROVEN–good to excellent results in 91% of 593 patients.[1]

WELL TOLERATED–side effects in these studies mild and temporary–incidence only 4.7%.[1]

INDICATIONS–For prevention or relief of the symptoms of allergic asthma, asthmatic bronchitis, chronic bronchitis with emphysema, emphysematous bronchospasm. Also for the relief of bronchial asthma associated with hay fever, allergic rhinitis and nonseasonal upper respiratory allergies.

DOSAGE–Adults: one tablet every 3 or 4 hours, four to five times daily. Children over six: one half the adult dosage. Available at all pharmacies.

FOR PROMPT EMERGENCY RELIEF **BRONKEPHRINE®** hydrochloride

(ethylnorepinephrine-Breon—10 cc. vials 2 mg./cc.)

"... far more than a substitute for epinephrine..."[2]

BREON **GEORGE A. BREON & CO., NEW YORK 18, NEW YORK**

1. Personal communication. 2. Foland, J. P.: Postgrad. Med. 18:397 (Nov.) 1955.

safety
efficacy
economy
rapidity
dependability
adaptability

Gantrisin... the quality of greatness

ROCHE

Reports in hundreds
of leading journals and
scores of standard textbooks
reflect the position of Gantrisin as drug
of choice in urinary and other bacterial infections.

ROCHE LABORATORIES

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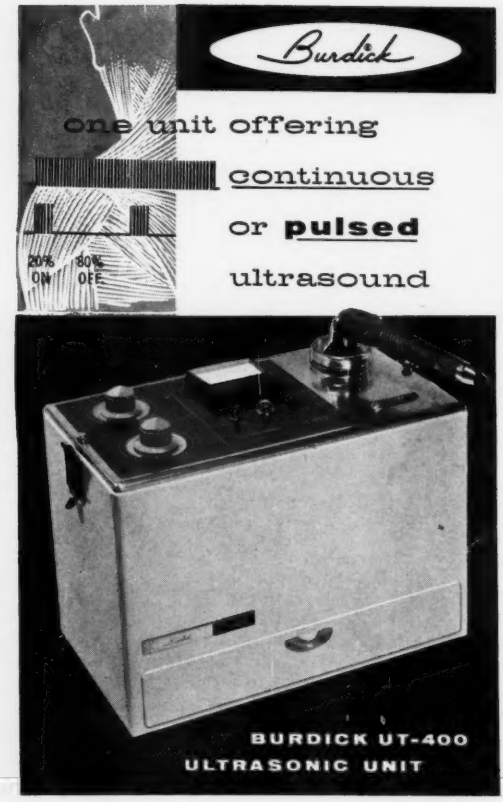
GANTRISIN®—brand of sulfisoxazole ROCHE®



Now, the all-new UT-400 provides *continuous* ultrasonic energy for conditions where both heating and mechanical effects are desired, or *pulsed* energy where a greater proportion of mechanical effect to thermal is indicated.

Although *continuous* ultrasound therapy is widely used throughout the country, *pulsed* energy is a relatively new development. Its advocates claim greater clinical effectiveness because the mechanical action can be increased with far less accumulation of heat. When the UT-400 is used for pulsed ultrasound, there is a duty factor of 20%.

Attractively housed in an aluminum cabinet measuring 16" wide x 12" high x 9" deep, the UT-400 weighs only 25 pounds complete with standard accessories. Total output: 21 watts (pulsed), 15 watts (continuous). Automatic timer switch.

Ask for a demonstration of the new Burdick UT-400 soon!

THE BURDICK CORPORATION
MILTON, WISCONSIN
Branch Offices: NEW YORK • CHICAGO • ATLANTA • LOS ANGELES
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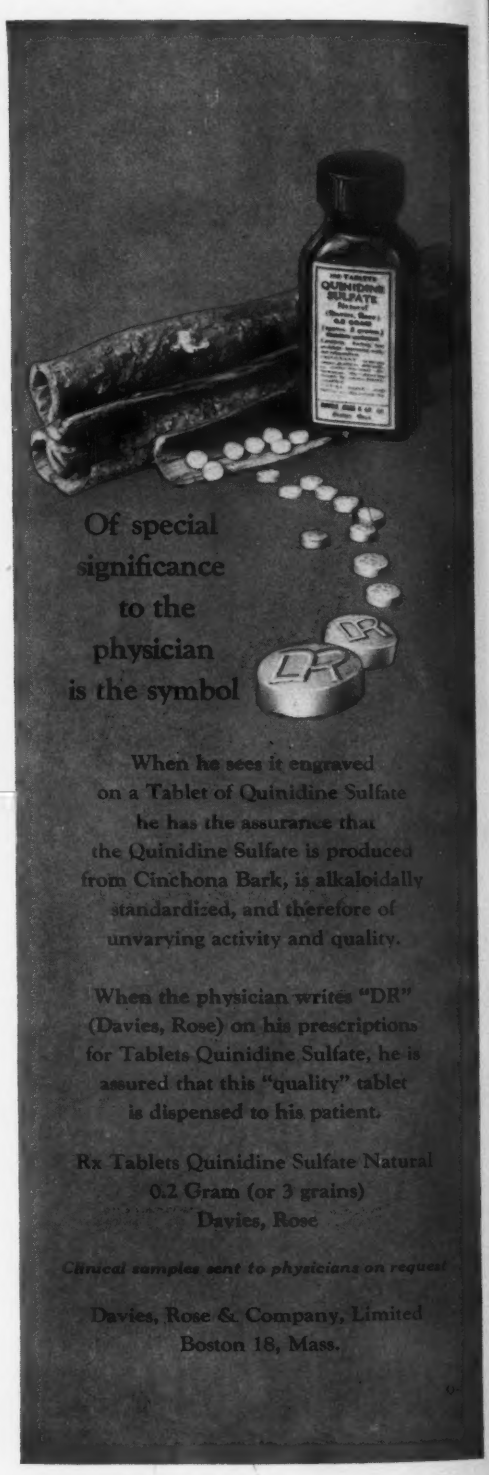

QUINIDINE SULFATE
Of special significance to the physician is the symbol
DR
When he sees it engraved on a Tablet of Quinidine Sulfate he has the assurance that the Quinidine Sulfate is produced from Cinchona Bark, is alkaloidally standardized, and therefore of unvarying activity and quality.
When the physician writes "DR" (Davies, Rose) on his prescriptions for Tablets Quinidine Sulfate, he is assured that this "quality" tablet is dispensed to his patient.
Rx Tablets Quinidine Sulfate Natural
0.2 Gram (or 3 grains)
Davies, Rose
Clinical samples sent to physicians on request
Davies, Rose & Company, Limited
Boston 18, Mass.

day and night—ulcer control with **B.I.D.** *dosage*

Just one 10 mg. Daricon tablet in the morning, and one at night before retiring, keeps your patient free from the pain and discomfort caused by gastrointestinal spasm, hypermotility, and hypersecretion.

Daricon is a remarkably potent and well tolerated antisecretory/antimotility agent. Its *naturally* prolonged action provides day and night relief of pain and symptoms associated with peptic ulcer, functional bowel syndrome, biliary tract dysfunctions, and other gastrointestinal disorders characterized by spasm, hypermotility, and hypersecretion.

EVEN REFRACTORY CASES RESPOND

new **DARICON***

oxyphencyclimine hydrochloride

Pfizer *Science for the world's well-being*™

Pfizer Laboratories
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

References: 1. Finkelstein, M., et al.: J. Pharmacol. & Exper. Therap. 125:330 (April) 1959. 2. McHardy, G., et al.: Postgrad. Med., in press. 3. Winkelstein, A.: Amer. J. Gastroenterol., in press. 4. Finkelstein, M., et al.: Presented at Fall Meeting, Amer. Soc. Pharmacol. & Exper. Therap., 1958. 5. Leming, B.: Clin. Med. 6:423 (March) 1959.

*Trademark

oral METRAZOL
reactivates the geriatric patient

oral METRAZOL
reactivates the convalescent

oral METRAZOL
reactivates the fatigued

dosage

for the geriatric patient - 2 tablets or teaspoonfuls, three times daily.
for the convalescent and the fatigued - 1 or 2 tablets or teaspoonfuls, three times daily.

availability

METRAZOL Tablets and Liquidum
Each tablet, 100 mg. METRAZOL. Each teaspoonful, 100 mg. METRAZOL and 1 mg. thiamine.

— for those patients who need additional vitamins —

Vita-METRAZOL Elixir and Tablets
Each teaspoonful, 100 mg. METRAZOL, 10 mg. niacinamide, 1 mg. each of thiamine, riboflavin, pyridoxine, and 2 mg. d-panthenol. Each tablet, in addition, 25 mg. vitamin C.

METRAZOL® brand of pentylenetetrazol, E. Bilhuber, Inc.

packaging
Tablets in 100's and 500's. Liquid (wine-like flavored 15 per cent alcoholic solution) in pints.

KNOLL PHARMACEUTICAL COMPANY
(formerly Bilhuber-Knoll Corp.)
Orange, New Jersey

Specific antitussive action of Narcotine affords selective control of the cough reflex.

● non-toxic ● non-habit forming
● free from side effects

RHINALL COUGH SYRUP

makes cough more productive

soothes bronchial irritation

Supplied: 3 oz. and pint bottle. Exempt Narcotic

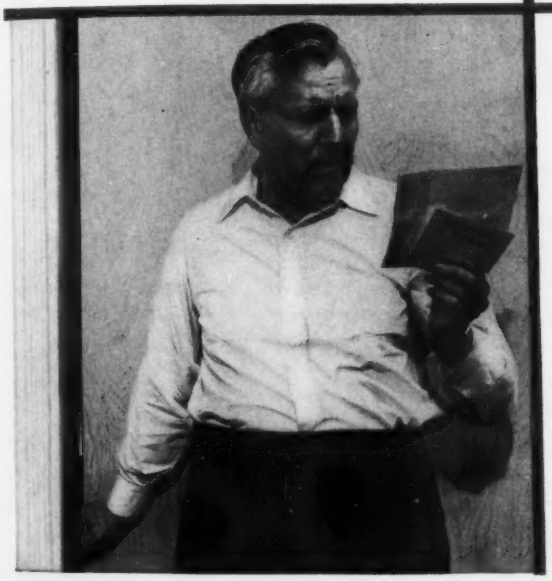
Each 5 cc. teaspoonful contains:

Narcotine	5.0 mg.
Phenylephrine Hydrochloride	5.0 mg.
Pyrilamine Maleate	12.5 mg.
Glyceryl Guaiacolate	50.0 mg.
Citric Acid	50.0 mg.
Sodium Citrate	22.5 mg.
Alcohol	5.0%

RHINOPTO COMPANY - Dallas, Texas

In Coronary Insufficiency...

Your high-strung angina patient often expends a "100-yd. dash" worth of cardiac reserve through needless excitement.



Curbs emotion as it boosts coronary blood supply

CONTROL OF EMOTIONAL EXERTION with Miltrate leaves him more freedom for physical activity.

IMPROVED CORONARY BLOOD SUPPLY with Miltrate increases his exercise tolerance.

Miltrate*

Miltown® (*meprobamate*) + PETN

Each tablet contains: 200 mg. Miltown and 10 mg. pentaerythritol tetranitrate.

Supplied: Bottles of 50 tablets.

Usual dosage: 1 or 2 tablets q.i.d. *before meals* and at bedtime. Dosage should be individualized.

® WALLACE LABORATORIES · *New Brunswick, N. J.*

CML-9199-59 *TRADE-MARK

In Asthma

The Most Important Word to Remember...

Medihaler

automatically measured-dose aerosol medications
Nonbreakable • Shatterproof • Spillproof • Leakproof

Available with either epinephrine or isoproterenol

Medihaler-EPI

Epinephrine bitartrate, 7.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each measured dose contains 0.15 mg. epinephrine.

Medihaler-ISO

Isoproterenol sulfate, 2.0 mg. per cc., suspended in inert, nontoxic aerosol vehicle. Contains no alcohol. Each measured dose contains 0.06 mg. isoproterenol.

NOTABLY SAFE AND EFFECTIVE FOR CHILDREN, TOO

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the addition of the decongestant makes for better cough control

by decongesting the cough area

while controlling the cough reflex

TRIAMINICOL provides more complete cough control than regular "cough syrups" because it contains Triaminic,[1,2,3] the leading oral nasal decongestant. This decongests the mucous membranes of the respiratory tract, reducing swelling and sensitivity, and controlling irritating postnasal drip, a common cough stimulus.

TRIAMINICOL also acts directly on the cough reflex center. It provides the nonnarcotic antitussive, Dormethan, fully as effective as codeine but without the drawbacks of codeine.[4] Liquefaction and expulsion of exudates is aided by the classic expectorant action of ammonium chloride.

References: 1. Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. 2. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 3. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958. 4. Bickerman, H. A.: in Drugs of Choice, Mosby, St. Louis, 1958, p. 547.

Each 5 ml. tsp. of TRIAMINICOL provides:

Triaminic® .....25 mg.
(phenylpropanolamine HCl .....12.5 mg.
pheniramine maleate ..... 6.25 mg.
pyrilamine maleate ..... 6.25 mg.)
Dormethan (brand of dextromethorphan HBr) .....15 mg.
Ammonium chloride .....90 mg.

In a pleasant-tasting, fruit-flavored, nonalcoholic syrup.

Dosage: Adults – 2 tsp. 3 or 4 times a day; children 6 to 12 – 1 tsp. 3 or 4 times a day; children under 6 – dosage in proportion.

Triaminicol® syrup

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extends the range of decongestion in COLDS

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TABLETS AND SYRUP

relieves both / upper respiratory congestion bronchial congestion

- **effective** because d-isoephedrine combines both nasal and bronchial decongestant actions[1]—together with the histamine blocking action of chlorpheniramine.
- **fast** . . . clears air passages in 10-20 minutes. Relieves stuffiness, swelling, discharge. Prevents excessive post-nasal drip and resulting night cough.
- **safe** . . . Laboratory studies reveal little effect on CNS or pressor stimulation.[2] Minimal daytime drowsiness or interference with sleep.

1. Aviado, D. M. et al: J. Pharmacol. & Exper. Therap. 122: 406-417 (Mar.) 1958. 2. Laboratory Report: Research Div, Chas. C. Haskell & Co., 1959.

TABLETS AND SYRUP for adults and children . . .

COMPOSITION:	Per tablet	Per 5 ml. syrup
Chlorpheniramine maleate	4 mg.	2 mg.
d-Isoephedrine HCl	25 mg.	12.5 mg.

DOSE: Tablets: Adults: 1 tablet 3 or 4 times daily. Syrup: Children: 3-6 yrs. ½ tsp. t.i.d.; 6-12 yrs. 1 tsp. t.i.d. Adults: 2 tsp. t.i.d.

AVAILABLE: Tablets: Bottles of 100. Syrup: Pint bottles.

CHARLES C. HASKELL & COMPANY, *Richmond, Virginia*

Continued from page 1164

Education Committee of the Upper Eastern Shore Heart Association.

New officers of the Maryland Radiological Society are as follow: Dr. Thomas Reid, Frederick, President; Dr. Nathan B. Hyman, Baltimore, Vice-President; Dr. Albert B. Shackman, Baltimore, Secretary; and Dr. John Howard Franz, Baltimore, Treasurer.

MISSISSIPPI

Mississippi doctors who will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are as follow: Drs. W. Byron Inmon, Jackson, Section on Obstetrics; George D. Purvis, Jackson, Section on Orthopedic and Traumatic Surgery; J. Darrell Smith, Jackson, Section on Pediatrics, and W. H. Parsons, Vicksburg, Section on Surgery.

MISSOURI

Missouri doctors presenting papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are Drs. William A. Knight, St. Louis, Section on Gastroenterology; Warren G. Stamp, St. Louis, Section on Orthopedic and Traumatic Surgery; Francis J. Burns, St. Louis, Section on Proctology; Charles Nicolai, St. Louis, Section on Urology.

Dr. Vernon E. Wilson, Acting Dean of the University of Kansas School of Medicine, has been appointed Dean of the School of Medicine at the University of Missouri. Dr. Wilson will succeed Dr. Gwilym S. Lodwick, who has been Acting Dean of the School of Medicine since the resignation of Dr. Roscoe L. Pullen on March 24.

Dr. A. Lloyd Stockwell has been elected President of the visiting attending staff of the Kansas City General Hospital.

Dr. Roland P. Ladenson, Columbia, has been installed as President of the Missouri Heart Association.

The Menorah Medical Center, Kansas City, announces the officers of the medical staff as follow: Dr. Harold Passman, President; Dr. Bela K. Kent, President-Elect; Dr. David Waxman, Secretary; and Dr. Alexander Lichtor, Treasurer.

Dr. Charles F. Grabske, Independence, has been installed as President of the Kansas City Heart Association.

The Kansas City Academy of General Practice has named Dr. George V. Feist, Kansas City, "General Practitioner of the Year."

The annual W. Scott Johnson Award has been awarded by the Missouri Public Health Association to Dr. Lynn M. Garner, Jefferson City.

Dr. Oliver W. Hasselblad, Kirksville, has been elected President of the American Leprosy Missions, Inc., a Protestant leprosy relief organization.

Continued on page 89

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Today she would prefer

TRICHOTINE®

for her most personal cleansing

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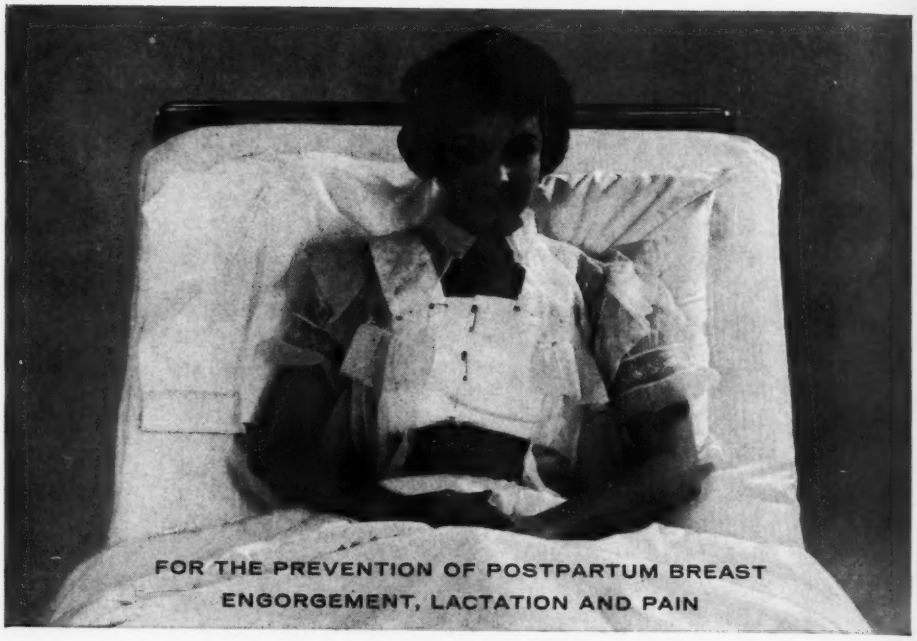

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(brand of methallenestril)

—avoids most withdrawal bleeding

—minimizes secondary breast symptoms and uterine subinvolution

—". . . causes fewer gastrointestinal upsets[1] than does diethylstilbestrol."

Schneeberg and his associates[2] gave Vallestril to 198 patients with postpartum breast engorgement, pain and lactation. They reported: "The patients . . . achieved over-all results . . . somewhat better than those in patients receiving 3 mg. of diethylstilbestrol. . . . Untoward effects, even when large doses were used, were rare. The 'slight bleeding' recorded . . . was probably of no significance and was doubtless no more than would have occurred in these individuals without therapy."

Napp, Goldfarb and Massell[3] conducted a controlled study in which 207 postpartum patients received Vallestril, 213 patients were given diethylstilbestrol and 193 patients did not receive hormone therapy. "The stilbestrol treated group showed a significantly greater incidence both of interim bleeding and of hypermenorrhea than did the control or the Vallestril treated groups."

These authors concluded that "Vallestril is a superior synthetic estrogen for the suppression of lactation. The low incidence of interim bleeding and of hypermenorrhea constitute a most important characteristic of the drug."

Only two 20-mg. tablets taken daily, for five days, suppress lactation and relieve engorgement and pain. Dosages for indications other than the suppression of lactation are given in Reference Manual No. 7. G. D. Searle & Co., Research in the Service of Medicine.

1. Council on Drugs: New and Nonofficial Drugs 1958. Methallenestril, Philadelphia, J. B. Lippincott Company, 1958, pp. 477-478.

2. Schneeberg, N. G.; Perczek, L.; Nodine, J. H., and Perloff, W. H.: Methallenestril, a New Synthetic Estrogen, J.A.M.A. 161:1062 (July 14) 1956.

3. Napp, E. E.; Goldfarb, A. F., and Massell, G.: The Parenteral Use of Methallenestril for the Suppression of Lactation. A New Approach, West. J. Surg. 64:492 (Sept.) 1956.

SEARLE

Continued from page 87

Dr. Richard A. Sutter, St. Louis, has been elected President of the Central States Society of Industrial Medicine and Surgery. Dr. William Macon, St. Louis, was elected to the Board of Governors.

Officers of the Kansas City Academy of General Practice are as follow: Dr. Harry K. Cohen, President; Dr. Frank A. O'Connell, President-Elect; Dr. J. Max Haight, Secretary; and Dr. Edward A. Samuelson, Treasurer.

Dr. Florence E. MacInnis, Kansas City, has been elected Medical Director of the Heart of America Tuberculosis Association.

Dr. E. A. Wilkinson is the new President of the Kansas City Surgical Society and Dr. Phillip Halperin is Secretary-Treasurer.

Dr. M. H. Black, Joplin, was elected President of the American Academy of Tuberculosis Physicians.

The newly elected members of the Board of Trustees of Group Hospital Service, St. Louis, are as follow: Dr. Carl S. Lischer, St. Louis, and R. Ned White, Springfield. Dr. M. K. Underwood, Rolla, was re-elected to the Board.

NORTH CAROLINA

Doctors from North Carolina who will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are: Drs. David A. Davis, Chapel Hill, Section on Anesthesiology; Joseph M. Hitch, Raleigh, and David G. Welton, Charlotte, Section on Dermatology and Syphilology; Malcolm P. Tyor, Durham, Marion D. Hargrove, and Frank Sohmer, Winston-Salem, Section on Gastroenterology; Leonard Palumbo, Chapel Hill, Section on Gynecology; Donald M. Hayes, Winston-Salem, Morton Bodonoff, Durham, and Ernest H. Yount, Winston-Salem, Section on Medicine; Leslie B. Hohman, Durham, Section on Neurology and Psychiatry; Charles N. Mauzy, Jr., Winston-Salem, Section on Obstetrics; S. D. McPherson, Jr., Durham, and J. C. Peele, Kinston, Section on Ophthalmology and Otolaryngology; James B. Wray, Winston-Salem, John S. Forrest, Durham, and William M. Roberts, Gastonia, Section on Orthopedic and Traumatic Surgery; Harry T. Zankel, Durham, Section on Physical Medicine and Rehabilitation; Glenn G. Perry, High Point, Section on Proctology; Edward G. McGavran, Chapel Hill, Section on Public Health; Thomas G. Thurston, Salisbury, Robert J. Reeves, Durham, and Robert S. Lackey, Charlotte, Section on Radiology; William R. Bosien, Tryon, Section on Surgery.

OKLAHOMA

The following Oklahoma doctors will present papers to the Southern Medical Association at its 53rd Annual Meeting which will be held in Atlanta, Georgia, November 16-19: Drs. Rene Menguy, Oklahoma City, Section on Gastroenterology; Elias Margo, Oklahoma City, Section on Orthopedic and Traumatic Surgery;

Continued on page 94

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Detergents are the modern, efficient way of cleansing. They provide greater surface activity and assure effective penetration.

Trichotine is the modern detergent vaginal douche. Unlike vinegar or low pH douches, Trichotine cuts through viscid leukorrheal discharge and allows complete penetration of its healing and soothing ingredients. Trichotine is bactericidal and promotes epithelization. It offers quick relief from pruritus, and its refreshing, soothing action is reassuring even to your most fastidious patients.

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? What is the diagnosis...

Mrs. X, age 35—physical findings negative.

Complaints: Constipation, alternating with periods of diarrhea, tenesmus, flatulence, colicky pains, easy fatigability, anorexia, periodic dull headaches and muscle pains.

Many times these symptoms point to *E. histolytica*, the parasite most often misdiagnosed,[1] and far more prevalent than generally suspected.[2,3,4]

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1. Elsdon—Dew, R.: S. Afr. Med. J. 32:89 (Jan., 1958)
2. Webster, B. H.: Am. Pract. & Dig. Treat. 9:897 (June, 1958)
3. D'Antoni, J. S.: New Orleans Med. & Surg. J. 102:55 (Aug., 1949)
4. Rinehart, R. E., Marcus, H.: Northwest Med. 54:708 (July, 1955)

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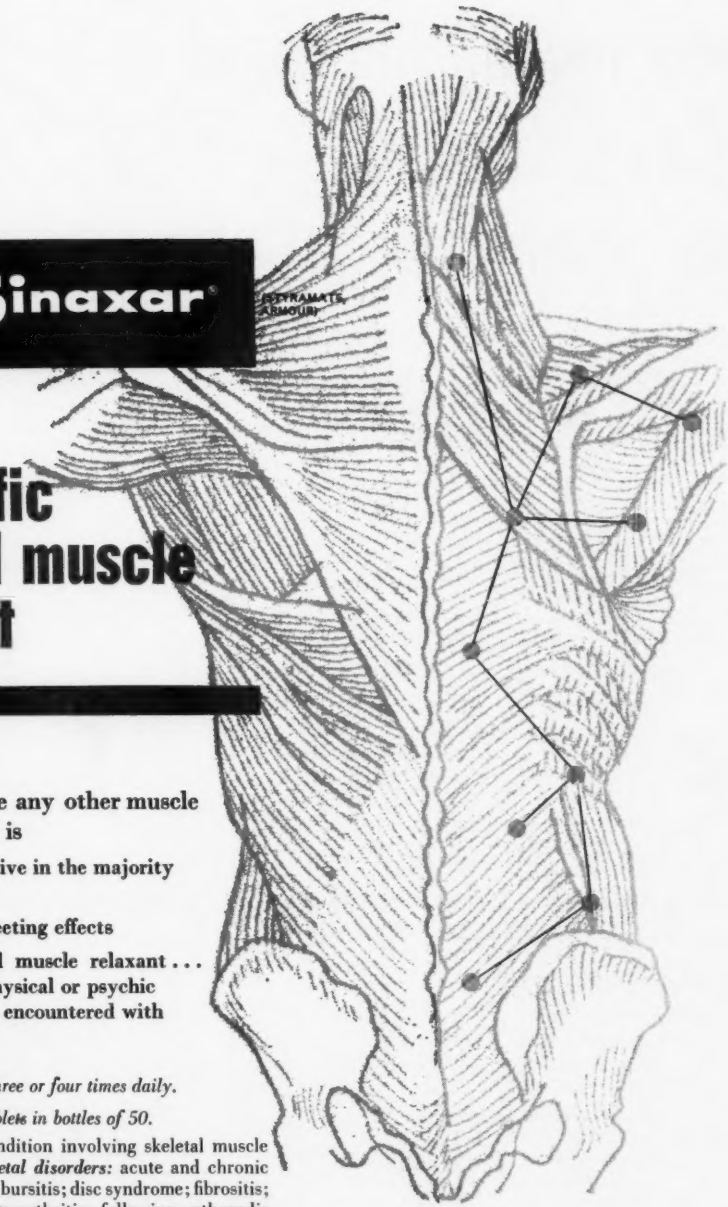

a specific skeletal muscle relaxant

Chemically unlike any other muscle relaxant, Sinaxar is

- **consistently effective in the majority of cases**
- **long acting: no fleeting effects**
- **purely a skeletal muscle relaxant . . . free of adverse physical or psychic effects frequently encountered with tranquilizers**

DOSAGE: *Two tablets three or four times daily.*

SUPPLIED: *200 mg. tablets in bottles of 50.*

INDICATIONS: Any condition involving skeletal muscle spasm, as *musculoskeletal disorders:* acute and chronic back ache; arthritides; bursitis; disc syndrome; fibrositis; myalgia; myositis; osteoarthritis; following orthopedic procedures; rheumatoid arthritis; spondylitis; sprains and strains; torticollis; *neurologic disorders:* cerebral palsy; cerebrovascular accidents; cervical root syndrome: multiple sclerosis.

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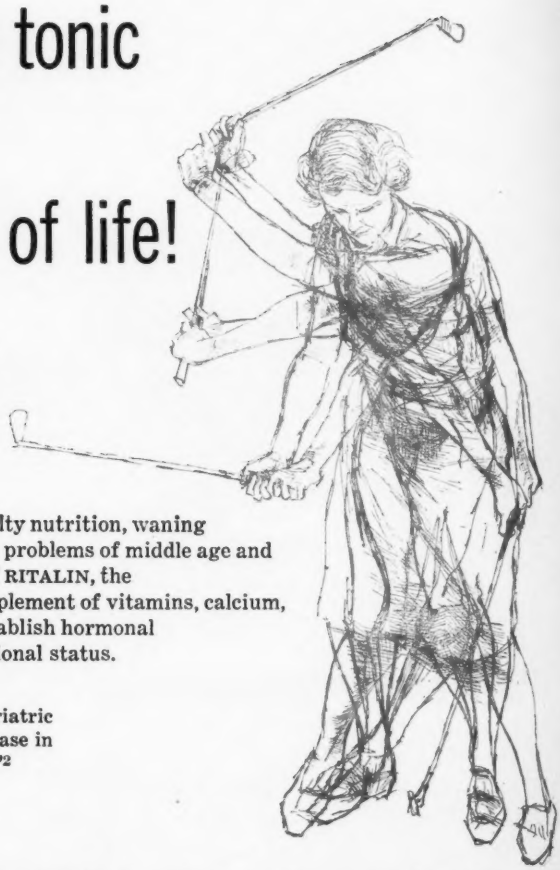

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A sense of frustration and inadequacy, faulty nutrition, waning gonadal function—RITONIC meets all these problems of middle age and senile let-down. The unique combination of RITALIN, the *safe* central stimulant, with a balanced complement of vitamins, calcium, and hormones acts to renew vitality, re-establish hormonal and anabolic benefits, and improve nutritional status.

"We found Ritonic to be a safe, effective geriatric supplement . . ."[1] "Patients reported an increase in alertness, vitality and sense of well being."[2]

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Ritalin® hydrochloride	5 mg.
methyltestosterone	1.25 mg.
ethinyl estradiol	5 micrograms
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dicalcium phosphate	250 mg.

Remember
SERPASIL®
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for the anxious hypertensive with or without tachycardia

Dosage: One Ritonic Capsule in mid-morning and one in mid-afternoon.
Supplied: Ritonic CAPSULES; bottles of 100.
References: 1. Natenshon, A. L.: J. Am. Geriatrics Soc. *6*:534 (July) 1958.
2. Bachrach, S.: To be published.
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Continued from page 89

Lucius Waites, Oklahoma City, Section on Pediatrics, and William W. Schottstaedt, Oklahoma City, Section on Public Health.

Dr. Henry T. Turner, Oklahoma City, former Councilor of the Southern Medical Association for the state of Oklahoma, was installed recently as President of the National Society of Nuclear Medicine in Chicago, Illinois. Dr. Turner has also been named Schering Scholar for this year by the American Endocrine Society.

The Oklahoma Eye Bank has been accepted as an affiliate of the Eye Bank for Sight Restoration, New York City. Only 14 other eye banks over the nation have met affiliation requirements. In the first year and a half of operation, the Oklahoma Bank has provided corneal material for 78 transplant procedures, but still has a long waiting list of patients.

SOUTH CAROLINA

South Carolina doctors who will present papers to the Southern Medical Association at its 53rd Annual Meeting which will be held in Atlanta, Georgia, November 16-19 are Drs. Morton L. Williams, Charleston, Section on Neurology and Psychiatry; and Leon Banov, Jr., Charleston, Section on Proctology.

Dr. John E. Zeliff, Greenville, has been certified by the American Board of Pediatrics.

Dr. John C. Bonner, Charleston, has been made a Fellow of the American Academy of Pediatrics.

Dr. W. R. Wallace, Chester, was recently honored by friends in celebration of his fifty years of practice in Chester.

TENNESSEE

At the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19, the following Tennessee doctors will present papers: Drs. Harold A. Schwartz, Chattanooga, and Bert H. Leming, Memphis, Section on General Practice; Samuel S. Binder, Chattanooga, Section on Gynecology; Glenn Clark, Memphis, Section on Medicine; Gene L. Whitington, Memphis, and R. L. DeSoussure, Memphis, Section on Neurology and Psychiatry; Phil C. Schreier, Memphis, Section on Obstetrics; J. William Hillman, Nashville, Section on Orthopedic and Traumatic Surgery; James T. Sweeney, Memphis, Section on Pediatrics; G. Turner Howard, Jr., Knoxville, Section on Proctology; Robert P. McBurney, Memphis, and Benjamin F. Byrd, Jr., Nashville, Section on Surgery.

Dr. Philip C. Elliott, Nashville, was elected President of the Tennessee Pediatric Society. Dr. Jack Mohr, Knoxville, was elected Vice-President and Dr. James Chesney, Knoxville, was named Chairman of the State Chapter of the American Academy of Pediatrics. Dr. George Lovejoy, Memphis, was elected Secretary-Treasurer.

Officers of the St. Mary Hospital staff include the

Continued on page 98

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ESTABLISHED 1916

An Institution for the diagnosis and treatment of Psychiatric and Neurological illnesses, rest, convalescence, drug and alcohol habituation.

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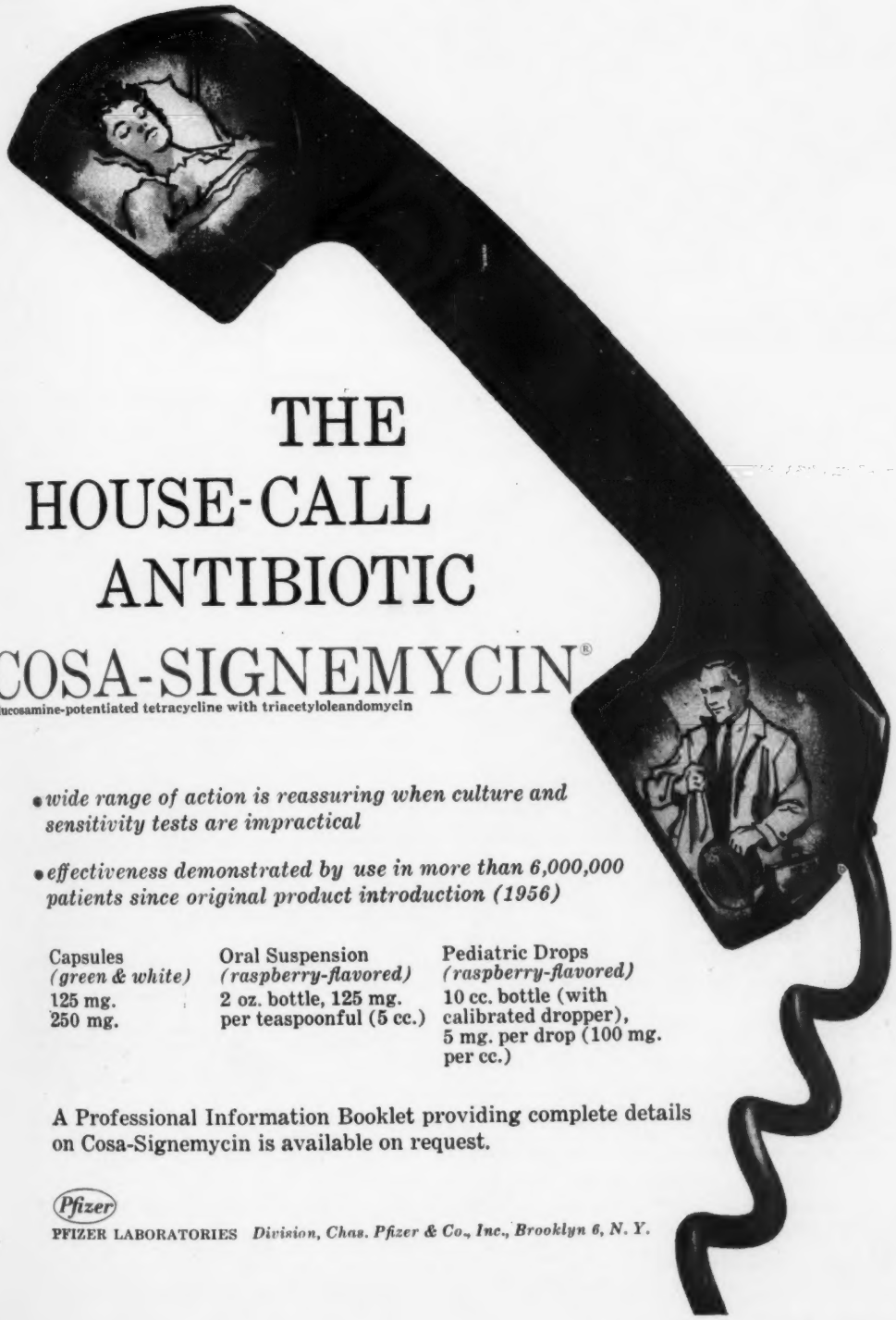

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125 mg. 250 mg.	2 oz. bottle, 125 mg. per teaspoonful (5 cc.)	10 cc. bottle (with calibrated dropper), 5 mg. per drop (100 mg. per cc.)

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Terpin hydrate .....180 mg.
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References: 1. Lhotka, F. M.: Illinois M. J. 112:259 (Dec.) 1957. 2. Fabricant, N. D.: E.E.N.T. Monthly 37:460 (July) 1958. 3. Farmer, D. F.: Clin. Med. 5:1183 (Sept.) 1958. 4. Bonica, J. J.: in Drugs of Choice, Mosby, St. Louis, 1958, p. 272. 5. Dascomb, H. E.: in Current Therapy, Saunders, Phila., 1958, p.78. 6. Bickerman, H. A.: in Drugs of Choice, Mosby, St. Louis, 1958, p.547.

Controls cough centrally
with non-narcotic Dormethan, possessing "amply demonstrated" antitussive activity,[6] as effective as codeine.

Liquefies tenacious mucus
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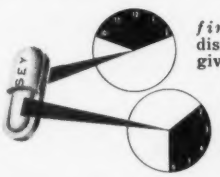

first — the outer layer dissolves within minutes to give 3 to 4 hours of relief

then — the inner core releases its ingredients to sustain relief for 3 to 4 more hours

Dosage: One tablet in the morning, midafternoon and at bedtime. Pediatric dosage chart for Tussagesic Suspension available on request.

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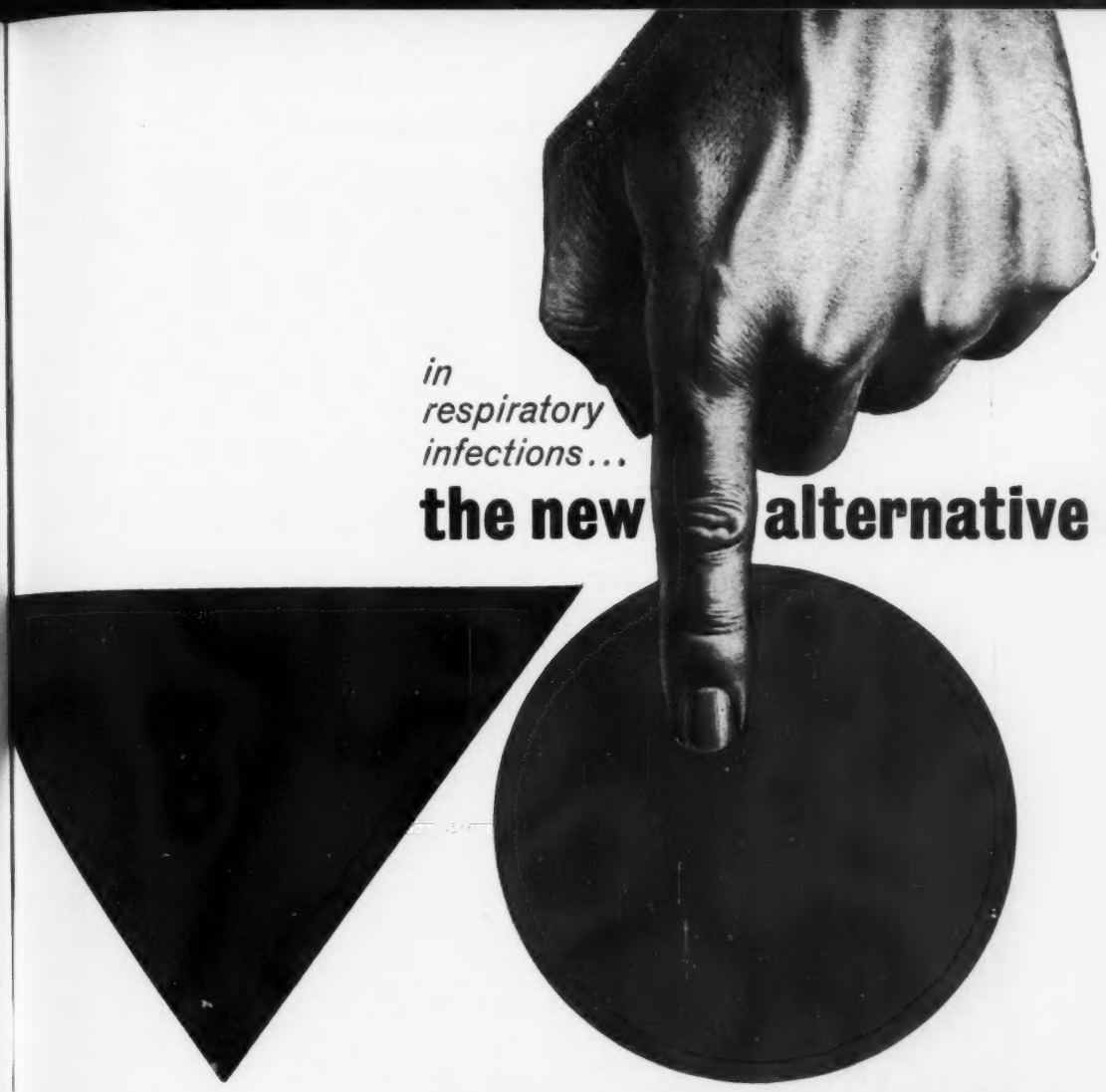

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DR. ROBERT K. WILLIAMS

Continued from page 94

following: Dr. H. G. Barker, Humboldt, President; Dr. F. Douglass, Dyer, Vice-President; and Dr. Eugene C. Crafton, Trenton, Secretary.

Dr. W. C. Crowder, Maryville, was elected Chief of Staff at Blount Memorial Hospital. Dr. John Yarbrough, Maryville, was chosen Vice-Chief.

Dr. Carl A. Hartung, Chattanooga, has been chosen a Fellow in the American College of Cardiology.

Dr. Walter K. Hoffman has been chosen President-Elect of the Memphis Heart Association. Dr. J. Warren Kyle is President and Dr. John P. Conway is Vice-President.

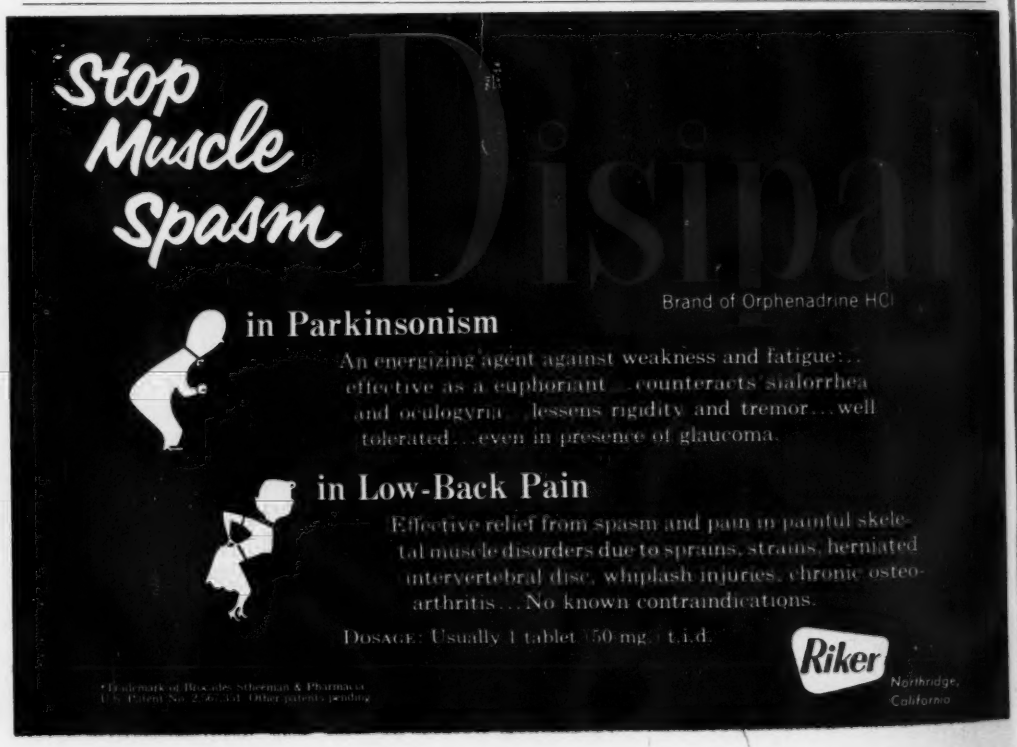
Dr. Estle P. Muncy, Jefferson City, has been elected President-Elect of the East Tennessee Heart Association.

Dr. Elliot V. Newman, Nashville, is President-Elect of the Middle Tennessee Heart Association. Dr. James J. Callaway was named President of the Association.

Dr. Samuel S. Riven, Nashville, is the President-Elect of the Tennessee Heart Association. Dr. Ben Hall, Johnson City, is the President for 1959, and Dr. Walter Huffman, Memphis, is Secretary.

Dr. Hollis E. Johnson, Nashville, was elected First Vice-President of the American College of Chest Physicians. Receiving Fellowship Certificates at the Convocation were Drs. E. Wayne Gilley, Chattanooga, and Douglas H. Riddle, Nashville.

Continued on page 100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Brand of Orphenadrine HCl
in Parkinsonism
An energizing agent against weakness and fatigue... effective as a euphoriant ... counteracts sialorrhea and oculogyria ... lessens rigidity and tremor... well tolerated... even in presence of glaucoma.
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Effective relief from spasm and pain in painful skeletal muscle disorders due to sprains, strains, herniated intervertebral disc, whiplash injuries, chronic osteoarthritis... No known contraindications.
DOSAGE: Usually 1 tablet (50 mg.) t.i.d.
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tablets · alka capsules

potent · nonhormonal · anti-inflammatory agent

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Recent clinical reports continue to justify the selection of Butazolidin for rapid relief of pain, increased mobility, and early resolution of inflammation.

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References: 1. Graham, W.: Canad. M. A. J. 79:634 (Oct. 15) 1958. 2. Robins, H. M.; Lockie, L. M.; Norcross, B.; Latona, S., and Riordan, D. J.: Am. Pract. Digest Treat. 8:1758, 1957. 3. Kuzell, W. C.; Schaffarzick, R. W.; Naugler, W. E., and Champlin, B. M.: New England J. Med. 256:388, 1957.

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*McLester, J. S., and Darby, W. J.: Nutrition and Diet in Health and Disease, ed. 6, Phila., Saunders, 1952, p. 195.

Continued from page 98

TEXAS

Texas doctors presenting papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are Drs. Albert H. Unger, El Paso, Section on Allergy; Eugene P. Schoch, Jr., Austin, Section on Dermatology and Syphilology; E. B. Best, Temple, Section on Gastroenterology; John T. Armstrong, Houston, Section on Gynecology; Ellard M. Yow, Houston, and George M. Jones, Dallas, Section on Medicine; W. L. Harlan, Galveston, W. P. Wilson, Galveston, and James B. Allison, Galveston, Section on Neurology and Psychiatry; John W. Simpson, San Antonio, Section on Obstetrics; Albert E. Meisenbach, Jr., Dallas, Section on Ophthalmology and Otolaryngology; W. J. Jinkins, Jr., Galveston, Section on Orthopedic and Traumatic Surgery; C. T. Ashworth, Dallas, Section on Pathology; Newton F. McDonald, Houston, and John T. Mallams, Dallas, Section on Radiology; John R. Derrick, Galveston, Section on Surgery; and Jasper Arnold, Houston, Section on Urology.

The Fifth District Chapter of Texas of the American College of Surgeons, Tenth District Medical Society of Texas, and the Beaumont Academy of Medicine will conduct a symposium on "Current Problems in Surgery and Medicine" September 19, in the Hotel Beaumont, Beaumont, Texas.

Continued on page 102

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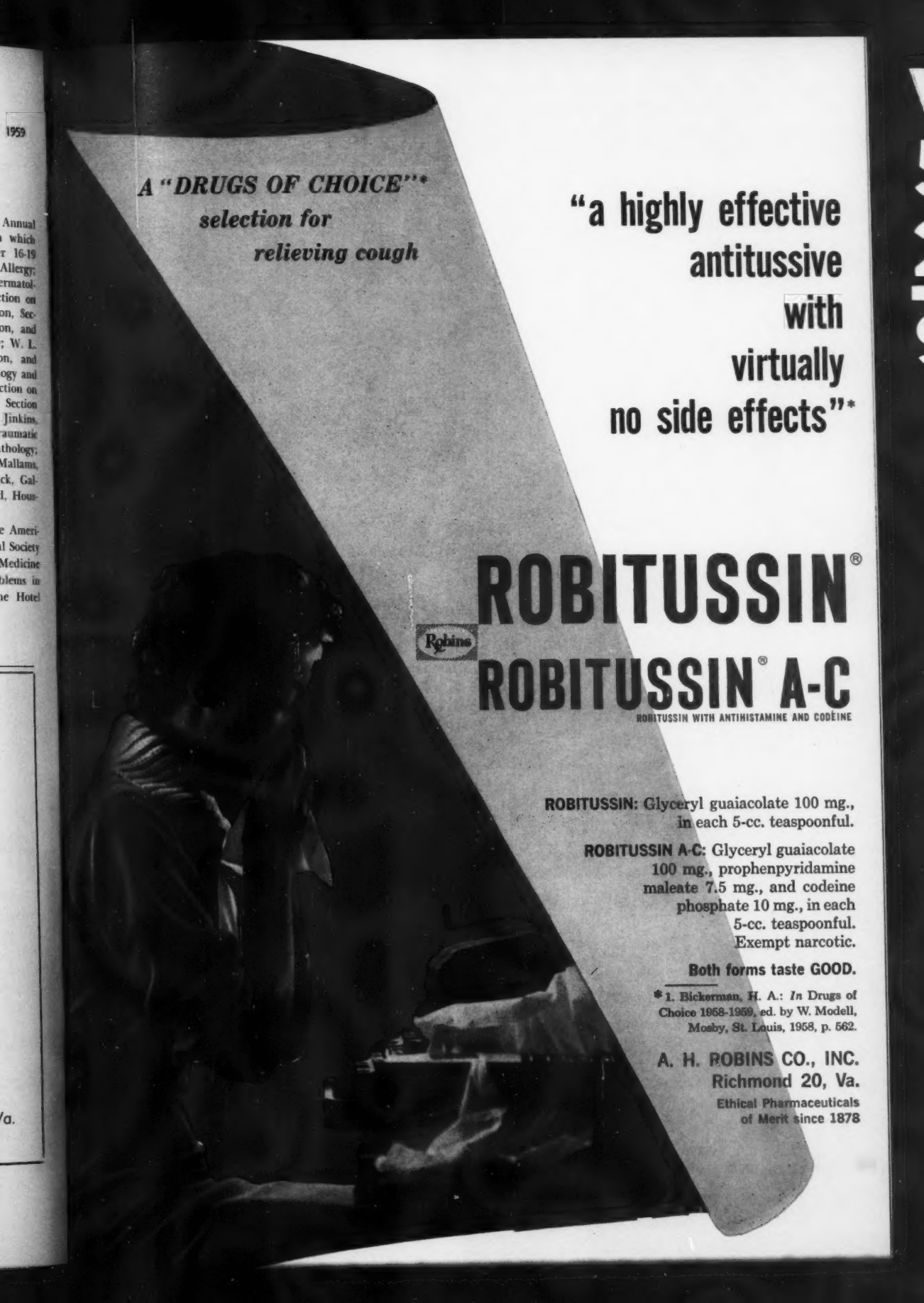
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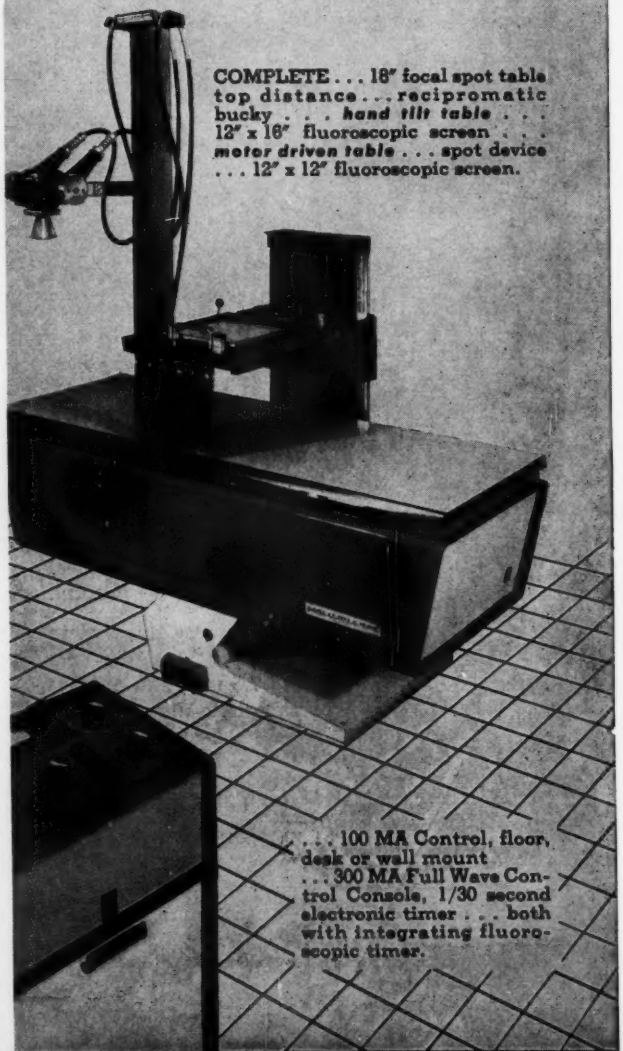

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Continued from page 100

The University of Texas Postgraduate School of Medicine announces that the James J. and Una Truitt Lecturer for the year 1959 will be Dr. Paul Wood, Physician in Charge of the Cardiac Department, Brompton Hospital, London.

Dr. Albert W. Hartman, San Antonio, has been elected President of the Southern Society of Clinical Surgeons at their recent meeting held in Baltimore.

VIRGINIA

Doctors from Virginia who will present papers at the 53rd Annual Meeting of the Southern Medical Association which will be held in Atlanta, Georgia, November 16-19 are Drs. Oscar Swineford, Jr., Charlottesville, Section on Allergy; Joseph C. Parker, Richmond, Section on Gynecology; G. S. Fitz-Hugh, Charlottesville, and Houston L. Bell, Roanoke, Section on Ophthalmology and Otolaryngology; William M. Deyerle, Richmond, Section on Orthopedic and Traumatic Surgery; McLemore Birdsong, Charlottesville, Section on Pediatrics; Herbert W. Park, Richmond, Section on Physical Medicine and Rehabilitation; Monford O. Custer, Jr., Winchester, Section on Surgery.

At the annual meeting of the Virginia Academy of General Practice, Dr. Fletcher J. Wright, Jr., Petersburg, was installed as President. New officers are as follow: Dr. Boyd H. Payne, Staunton, President-Elect; Dr. William H. Hagood, Jr., Clover, Vice-President; Dr. Samuel F. Driver, Roanoke, Secretary; and Dr. Irwin Rifkin, Richmond, Treasurer.

Dr. Ben C. Jones, Jr., has been installed as President of the Alexandria Medical Society. Dr. F. Preston Titus

Continued on page 106

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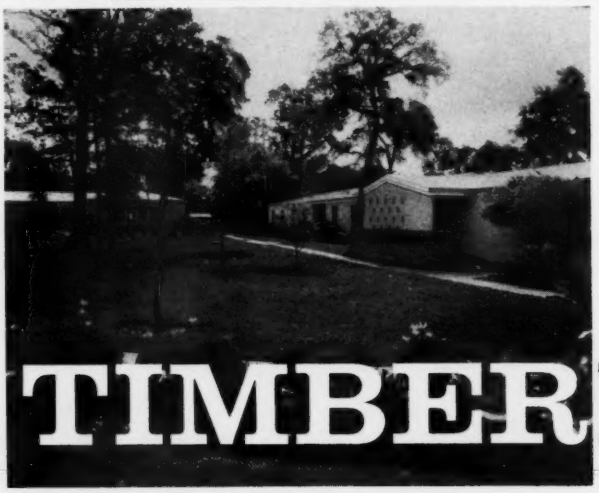

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Continued from page 102

was chosen President-Elect. Other officers are Dr. James Gilber, Vice-President; Dr. Walter J. Brennan, Secretary; and Dr. William H. Young, Jr., Treasurer.

New officers of the Norfolk County Medical Society are Dr. W. W. Taylor, President; Dr. John Franklin, President-Elect; Dr. Donald Faulkner, Vice-President; Dr. William Hotchkiss, Treasurer; Dr. M. I. Krischer, Recording Secretary; Dr. R. B. Guinnan, Local Councilor; and Dr. George Elsasser, Corresponding Secretary.

The Virginia Surgical Society announces its new officers as follow: Dr. Edmund Horgan, Winchester, President; Dr. Benjamin Rawles, Jr., Richmond, Vice-President; Dr. Robert L. Payne, Jr., Norfolk, Secretary; and Dr. William R. Hill, Richmond, Treasurer.

Dr. Carolyn McCue has become the first woman to be elected to the post of President of the Richmond Area Heart Association. Dr. Robley D. Bates, Jr., will be Vice-President.

Dr. John A. Sims is President of the Alexandria-Arlington Tuberculosis and Health Association.

Dr. Warren Gregory, Winchester, has been elected Chairman of the Northwestern Guidance Center. Dr. H. P Maccubbin is Secretary-Treasurer.

Dr. Leon W. Powell, Jr., Danville, was named Chief Pathologist at the Memorial Hospital. He will also serve as Director of the Hospital's laboratory.

Dr. James M. Suter, Abingdon, has been elected President of the Virginia Public Health Association. He is Southwest Regional Director of Local Health Services for the State Department of Health.

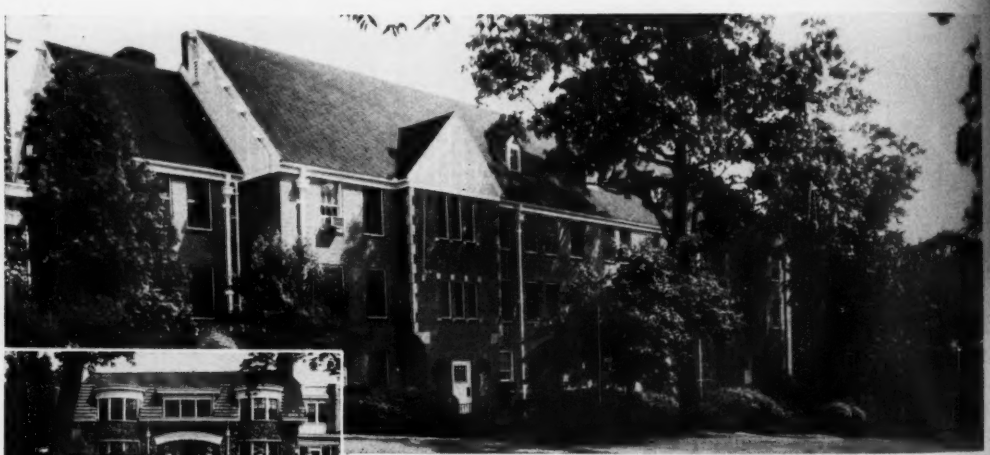
WEST VIRGINIA

Dr. Charles Newland Slater, Clarksburg, has been selected by the Council of the West Virginia State Medical Association as West Virginia's "General Practioner of the Year." Dr. Slater, now in his 80th year, still maintains active practice in Clarksburg. Dr. Slater was one of the first members both of the Southern Medical Association and the American Academy of General Practice.

The Barbour-Randolph-Tucker Medical Society announces its new officers as follow: Dr. Samuel C. Johnson, Parsons, President; Dr. John L. Rittmeyer, Phillipi, First Vice-President; Dr. A. C. Thompson, Second Vice-President; Dr. Charles L. Leonard, Elkins, Secretary; and Dr. Harold L. Jellinek, Elkins, Treasurer.

The Fort Henry Academy of Medicine announces the following officers: Dr. H. T. Phillips, Jr., President; Dr. T. O. Dickey, McMechen, Vice-President; Dr. William Perilman, Wheeling, Secretary-Treasurer; and Dr. George R. Clark, Program Chairman.

Dr. L. A. Lyon, Wheeling, was elected President of the Ohio County Medical Society recently. Other officers are Dr. A. K. Butler, Vice-President; Dr. R. W. Leibold, Secretary; and Dr. William Perilman, Treasurer.



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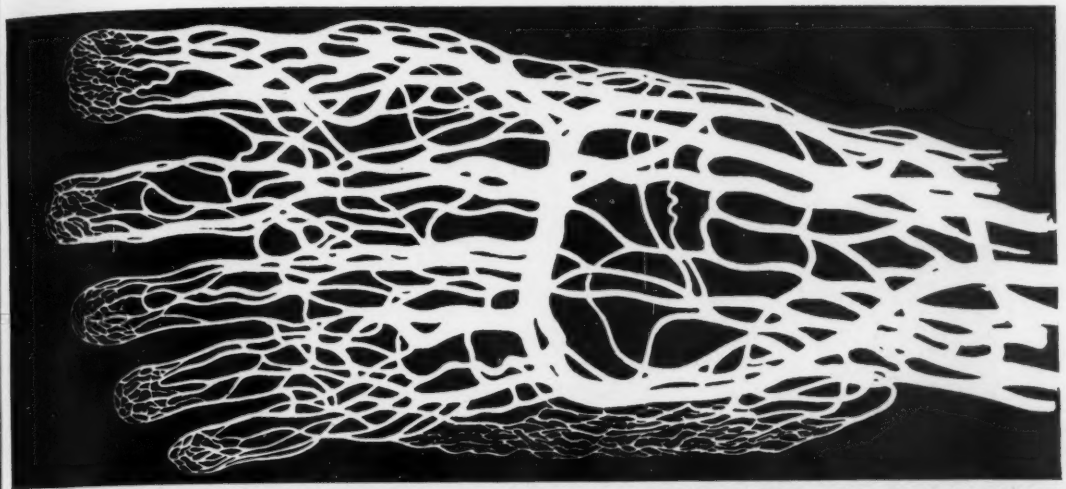

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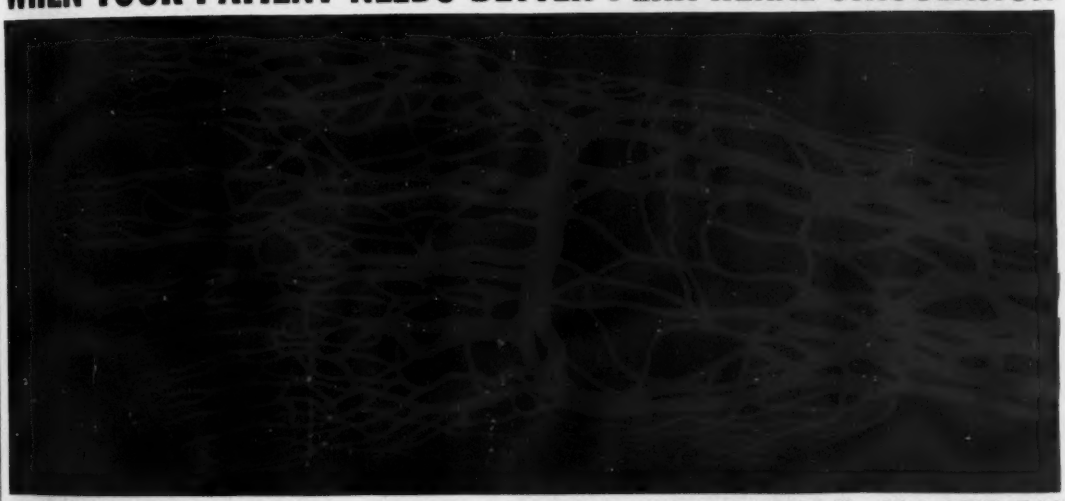

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1. Spies, T. D.: The Influence of Nutritional Processes on Aging, South. M. J., *50*:216, 1957.

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